The New England
Journal of Medicine

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Volume 237 NOVEMBER 20, 1947 Number 21

# OCCUPATIONAL DERMATOSES (ERGODERMATOSES)*

## Diagnosis, Disability and Treatment

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TWENTY minutes is rather a brief period in which to discuss the large field of industrial dermatoses, but a few thoughts resulting from twenty-five years' experience may be of interest. During that time many thousands of workers with cutaneous disturbances have been examined; key industrial plants have been inspected, and lectures have been given to workers, foremen and insurers. Most of the cases considered industrial have been treated; therefore, considerable experience has been gained by trial and error. No set rules have ever been established for the treatment of such dermatoses. The industrial patient must be treated until he is well; there is no reason why he should not recover, because all true occupational dermatoses are curable.

In Massachusetts in 1922 little was known about the effects of industrial exposures, but with the rapid introduction of new chemicals, insurers and industrialists soon learned that the resulting cutaneous disturbances were numerous and expensive. Industry in the Commonwealth has changed in the last twenty-five years. Old industries are gone, and new ones have been installed. Formerly, the leather industry was responsible for a large amount of workers' disability due to occupational dermatoses; later, the rubber industry contributed quite a few cases. The former moved away, and the latter cleaned house. As a result of prophylactic measures, industries formerly notorious for causing dermatoses now have only an occasional worker affected.

The first cases of dermatitis from work with plastics were seen in a small plant in a large field; it is now such a large plant that the field seems small. When this plant was first visited, it was dusty and reeked of fumes. Finished fabricated plastics, being inert, do not cause dermatoses, but the processing of the raw materials produces a considerable number of cutaneous reactions. There is a dangerous combination of powders, liquids and gases. Although plastics have been made as long as clay has been known, the use of resins resulting from the reaction of phenol and formaldehyde and similar reactions is only thirty years old. The pruritic eruption due to mechanical irritation from the powders has been fairly well eliminated by improved personal hygiene, better washing facilities and the use of protective creams. Education has eliminated skin conditions caused by the careless handling of liquids, which ranged from simple follicular eruptions to severe burns. Lastly, proper sanitation has eradicated not only the helmet-like type of dermatitis on the exposed areas of the skin caused by fumes but also the fine papular eruption resembling prickly heat that appeared on the covered areas, especially in warm weather, owing to penetration through the clothing. There was a constant change of personnel, for whereas many became desensitized, others had to give up this work. Those now affected are new and inexperienced workers.

Lectures accomplish a great deal, but money talks more successfully. Insurers, recognizing the bad risks, drop these policies, and the next insurer raises the premium. A worker with an occupational rash is an expensive liability, especially in these days of high-cost hospitalization. Apart from the loss of time and wages of the employe, the compensation and medical expenses may amount to several thousand dollars. A mild eruption may cost at least two or three hundred dollars.

The introduction of patch tests was hailed as the solution to this puzzle (Fig. 1). Insurers began to insist on them, commissioners requested them, and patients consented to submit to them. After a decade of enthusiasm, however, patch tests have lost much of their popularity, owing to the number of false or severe reactions (Fig. 2). They are now relegated to their proper use — that is, only when indicated. They have their fallacies and limitations, but with a carefully taken history showing definite exposure to the test material, and with a characteris-

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 20, 1947.

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tic test eruption, a positive finding followed by the prevention of further exposures should result in a cure.[1]

Years ago most workers attributed every eruption to their work. Skilled employes soon realized that alleged industrial hypersensitivities were disastrous, physically and financially, and demanded proof of the causative factor. The physician became more careful in his diagnosis of an occupational dermatitis, for the well paid artisan is apt to resent any loss of pay when it is proved that his eruption is not due to his work but is constitutional in origin or is due to contacts at home, especially when industrial commissioners so rule against him. With the recent increase in wages, workers became suspicious of snap diagnoses, and it is amazing how many continued to work despite their occupational eruption and were relieved without loss of time.

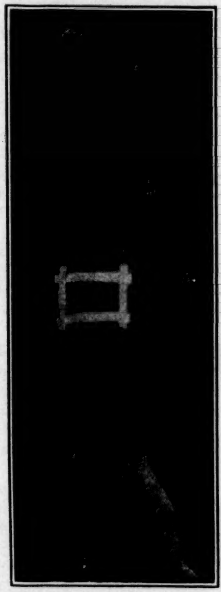

FIGURE 1. *Method of Patch Testing.*[1]
*A piece of linen is moistened with the test substance and covered with Scotch tape that is rimmed with narrow adhesive.*

Despite the tremendous increase in industrial activities during World War II, the increase in dermatoses was not excessive in this part of the country, except in the incidence of infection due to cutting oils. The increase occurred for the most part in plants transformed overnight into machine shops. The incidence of claims for industrial dermatoses is an excellent index of industrial productivity. For the past two months there have been more claims than in any two months when wartime activities were at their height.

## DIAGNOSIS

What establishes the diagnosis of an occupational dermatosis? In 1939 the Committee on Industrial Dermatoses of the American Medical Association[2] adopted the following definition: "An occupational dermatosis is a pathological condition of the skin for which occupational exposure can be shown to be the major causal or contributory factor." The same committee submitted the following criteria, which usually apply in the majority of cases of occupational dermatoses:

The dermatologic diagnosis is that of a dermatosis in which the role of an occupational causal (major or contributory) factor has at some previous time been established beyond reasonable doubt.

The patient has been working in contact with an agent known to have produced similar changes in the skin.

The time relation between exposure to the agent and the onset of the dermatosis is correct for that particular agent and that particular abnormality of the skin.

The site of the onset of the cutaneous disease and the site of maximum involvement are consistent with the site of maximum exposure.

The lesions present are consistent with those known to have followed the reputed exposure or trauma.

The patient is employed in an occupation in which similar cases have previously occurred.

Some of the fellow workers using the same agent are known by the examiner to have similar manifestations from the same cause.

So far as the examiner can ascertain there has been no exposure outside the occupation that can be implicated.

If the diagnosis is dermatitis, the following items are important: attacks occurring after exposure to an agent, followed by improvement and clearing after cessation of exposure, constitute most convincing evidence of the occupational factor as a cause; and the results of patch tests performed and interpreted by competent dermatologists corroborate the history and the examination in the majority of cases.

These criteria, however, are rather complicated and do not apply to cases in which there is aggravation of an existing cutaneous disease by industrial exposure. Nor do they apply to the large number

of cases in which the disabling eruption has resulted from treatment by the plant physician or nurse with a sensitizing medicament or has been caused by overtreatment.

## Medicolegal Aspects

In Massachusetts the legal definition of occupational dermatosis seems more clear-cut. It is any injury, damage, harm or disease of the skin that arises out of and in the course of employment.[3] Such an injury is compensable if it causes incapacity and takes away a worker's ability to earn wages. Disease is not compensable unless it arises from an injury, and although dermatitis is considered a disease, definite injury must be established before a claim is accepted. These facts are simple but are misinterpreted, not only by the general practitioner but also by the dermatologist. A recent article written by a dermatologist stated that miliaria was considered occupational if the weather was hot. (Miliaria is an acute affection of the sweat glands that occurs in many persons in hot weather, regardless of whether or not they work.) A new industrial commissioner dreads a case of dermatitis, and few private lawyers have any understanding of the Compensation Act or of the court decisions regarding it. Many a plaintiff would have lost his claim except for a sympathetic commissioner. These officials are admittedly slightly partial to the employe, and perhaps justly so. To the insurer and its representatives, either lawyers or physicians, it is just another case, the loss of which will not in any way change their routine. To the injured worker it is a tragic, all-absorbing controversy, the solution of which may determine his future and that of his family.

Cases of occupational dermatoses are so complicated that the Massachusetts Industrial Accident Board will not accept an opinion unless it is expressed by a duly qualified physician. What makes these decisions so difficult? It is because few have the training that enables them to assemble all the parts and solve the problem. A physician must have dermatologic training to distinguish between the occupational and the nonoccupational dermatoses. In reviewing many thousands of cases of workers presenting claims, I found about 40 per cent to be nonindustrial; comparatively few of these opinions have been disputed. Correct dermatologic diagnoses save employers, insurers and employes many thousands of dollars. A knowledge of occupational exposures is essential, including the chemicals used and the processes involving their use. A knowledge of the sanitary conditions in a particular plant is helpful. For example, fungous infection of the feet is not considered industrial, but, if a man is constantly working on a wet or damp floor so that his shoes and socks are always wet, an ideal condition is produced for the growth of yeast and fungi and could be a precipitating factor in a disability that later results from this infection.

Thorough examination of the claimant is essential. The sites first affected and the characteristics of the eruption should establish a definite diagnosis of an occupational dermatosis. These facts are few, but each one has its own importance in the expression of an opinion. The physician needs no vast knowledge of chemistry or sanitation to gather all his data, because on request the insurer as a rule will supply this information; if not, the various state agencies are willing to assist him.

Figure 2. *Case of J. T., a Candy Maker (Dermatitis from Contact with Cinnamon Oil).*

*The patch test resulted in a generalized dermatitis.*

There are a large number of cases in which the worker acquires a superficial injury of the skin, such as a paper cut, abrasion or friction burn, and later suffers a pyogenic infection at this site, showing a sharply outlined vesicular and pustular eruption that is resistant to treatment and subject to frequent relapses. These cases are often mislabeled "fungous infection" owing to failure to obtain a history of injury or cultural studies, and the worker is refused compensation. The largest group, however, comprises patients overtreated or treated with medication to which they have a hypersensitivity. This medication was formerly a mercury compound, later the sulfonamide group, and next penicillin, and I have recently seen 2 cases resulting from the use of Furacin. These drugs should not be employed in occupational dermatoses unless there is infection, and then with caution and only until the secondary infection is relieved, when bland medication should be substituted.

FIGURE 3. *Case of S. D., a Leather Seasoner (Chromic Acid Burns).*

*The lesions (seen in tanners, masons and plasterers) show an elevated rim of whitish-gray skin with a central dark ulceration resembling a pigeon's eye, and hence called "pigeonneau."*[4]

## HYPERSENSITIVITY

The majority of true occupational dermatoses are due to primary skin irritants. In 1936 the committee mentioned above defined a primary irritant as follows: when a substance in a given concentration, in a given vehicle and in a given manner and length of exposure produces a clinically manifested irritation on the skin of a majority of persons not previously sensitized to that substance, that substance is a primary irritant under the specified conditions.[3] Irritants may cause lesions ranging from erythema to deep necrosis of the skin (Fig. 3). Primary irritants can comprise mechanical and physical agents and powerful chemicals, including acids, alkalies, metals, salts, essential oils, solvents and miscellaneous substances.[5] In this large group of cases, the history should reveal the causative factor, because patch tests are unnecessary. Primary irritants should not be used in patch testing. Again, most of the workers suffering from the above conditions can continue to work unless the eruption is severe; when it has disappeared, there is no reason why they should not return to their previous occupation.

It is essential to distinguish between primary skin irritants and sensitizers, frequently called "allergens" or "allergenic substances." The Committee on Industrial Dermatoses has defined a sensitizer as one that increases the capacity of the tissue to react to subsequent exposure. In my experience hypersensitivity to a single allergen occurs in only a few industries. This group of sufferers constitutes the chief problem in occupational dermatology. A carefully taken history of any previous cutaneous disease is most important; in my experience, about 7 per cent of patients have had previous attacks.

FIGURE 4. *Case of J. S., a Leather-Heel Trimmer. Sensitization produced an eruption simulating nummular eczema.*

Primary irritants that are also sensitizers are essential oils, acids (carbolic, chromic and oxalic) alkalies, soap, cement, lime, various salts — such as the chromates, sulfates, arsenates and nitrates — solvents and the miscellaneous group previously mentioned (Fig. 4). The variation of the incuba-

tion period is misleading: it may range from several days to many years. In this group patch tests may be of value, and the patient usually has to seek other employment. The longer the incubation period or time of exposure, the greater the sensitization and the more difficult the cure, because these patients become polysensitized. Therefore, medication must be carefully selected, outside activities curtailed, the use of soap and water prohibited and even a dietary regime imposed, for the use of stimulants and improper diet prolongs the disability. The onset is slow and insidious, and the skin frequently presents a somewhat characteristic appearance; except for the hypersensitivity, there is no permanent stigma, such as scarring. This hypersensitivity does not remain specific.

The workers become subjects of controversy before industrial-accident boards for the rest of their occupational existence. They are the ones told not to return to their previous occupation and to avoid exposure to wet work and the use of soap and water — in other words, to refrain from some of the normal activities of life. By law, this hypersensitivity is not compensable; the worker must seek other employment and avoid the substance that might produce a new attack. If this new attack occurs at home or under self-employment, there is no redress; if it occurs while he is working for a new employer, the responsibility for medical care and compensation rests on him. If the worker testifies under oath that some traces of the original eruption remain over a period of several years, the original employer or his insurer is responsible. It sounds simple, but clever lawyers can make the rendering of an impartial decision extremely difficult. The injured employe listens, dazed with the conflicting testimony. He may, however, amaze the attending physician, employed by the insurer, who, properly proud of having cured a difficult eruption, has to listen to criticism of his efforts and accusations against his integrity. The timely use of soap and water or chemicals or friction just before the hearing is sometimes a matter of consternation to the attending physician, who a few days or weeks previously had reported that the patient was well. During the war these cases were extremely rare, but now they are increasing and occur mostly among female workers who have returned to the role of housewives or who have married and find the compensation a useful adjunct to the household budget. Perhaps there is some justification for their position, but we must realize that the largest group of occupational dermatoses is among housewives, who comprise nearly 30 per cent of my private practice; practically all these cases are due entirely to household activities, exposure to soap and soap powders, squeezing oranges, handling raw vegetables and fruit, canning and many of the other activities of the active mother (for 95 per cent of these women have children). These are persons who have never had outside industrial contacts, so that it is just as probable that the plaintiffs were victims of their own household exposures. I believe that the proper way to dispose of these cases would be a reasonable lump-sum settlement, for as O'Donovan[8] states there is nothing more curative than the golden ointment of compensation.

Characteristic lesions may appear from exposure to these sensitizers or allergens, producing the so-called "allergic dermatitis" or eczema. These are inflammations of the skin due to repeated exposure to substances that are normally innocuous (Fig. 5).

FIGURE 5. *Case of H. M., a Shoe Dresser.*

*Eruption frequently seen in shoe dressers and treers from contact with irritating chemicals.*

Chlorinated hydrocarbons usually produce characteristic mechanical and follicular plugging with comedones and cysts, but occasionally an allergic reaction consisting of a diffuse erythema is seen on the face, hands and arms of chemists after repeated experimentation. This erythema fades, the skin desquamates, and finally the characteristic comedones and cysts appear as the result of condensation of chloro compounds in the follicles. A similar combination of mechanical or primary irritation and sensitization reaction is seen in workers who use soluble cutting oils. The sensitization is due to the sulfuric acid and the preservatives in the oils.

Resins and sensitizing dusts frequently cause symptoms and signs similar to those produced by cosmetics, such as face powders and nail polish.

There is itching of the eyelids and the sides of the neck; later, other parts of the exposed skin become affected. The skin is dry, red and scaly, and continued exposure causes edema of the eyelids. As the patient becomes more sensitized the edema appears, and fine papules and vesicles are superimposed.

Workers whose hands are constantly wet develop maceration of the interdigital skin and a sensitivity to the chief ingredient in the solution, whether it is soap, a fruit or a vegetable. I have seen positive patch-test reactions from carrots, lettuce and tomatoes. These eruptions usually start in the webs of the fingers and spread over the backs of the hands and on to the anterior aspect of the wrists. There is a "boiled-out" appearance of the interdigital interspaces, with erythema and vesiculation of the remaining areas. The eruption rarely spreads beyond these areas unless overtreated, and is usually complicated by secondary infection, such as pyogenic bacteria or yeastlike organisms.

Sensitivity to chromates and bichromates, which may be polymorphous in character, presenting oval or round patches, is frequently seen in shipyard workers in contact with a dull-green paint. These patches are described by Hall,[7] who attributes them to contact with the zinc chromate primer in the paint. He was able to differentiate the eruptions from zinc chromate and those from resin. The latter causes a dermatitis on the sides of the neck, consisting of oval, dull-red, finely squamous, palpable plaques whose long axes are parallel to the lines of cleavage of the skin, as in pityriasis rosea, whereas the former causes nummular and eczematous plaques. The most interesting eruption was one seen at the beginning of the recent war among the enlisted personnel in the Navy and Coast Guard. It appeared on the dorsa of the hands, near the wrists, and on the outer lateral aspects of the extremities. The primary lesions were vesicles, which later became grouped, forming elevated, circular, red, vesicular and oozing patches that tended to clear in the center. These eruptions resembled nummular eczema and were frequently so diagnosed. Patch tests proved that they were caused by the cloth of the uniform, due to a bichromate used as a mordant. A similar eruption appeared among stitchers of this cloth.

Workers highly sensitized to gasoline may show a generalized eruption consisting of erythema and patches of grouped vesicles similar to a dermatitis herpetiformis. Male workers in garages and places where there are poor working conditions, such as dirty floors, frequently present eruptions that start on the dorsa of the feet and about the ankles, spreading up the legs. Rubber finger cots may cause an intensely pruritic, pink, scaly eruption at the site of contact, and heavy rubber gloves may cause a colorless, fine, papular eruption. Dye may produce nothing but an intense edema followed by desquamation. Even the most expert diagnosticians, however, cannot depend alone on observation, for most contact eczemas are similar in appearance, and a complete history and patch testing are usually necessary to prove the original cause. When other cases result from the same exposure, the cutaneous disturbance is readily recognized. Experience is the best teacher.

## Disability

All insurers' medical reports request that the physician express an opinion regarding disability — whether it is total or partial, permanent or temporary. What constitutes disability? The insurer recognizes the fact that if an injury occurs in the course of employment and produces an extensive dermatitis, the worker is temporarily totally disabled. When the accomplishments of blind veterans and those without limbs are considered, however, it seems incongruous to state that the dermatitis of the right index finger of the maker of rubber coats is totally disabling. But this injury destroys his earning capacity, for his work is done chiefly with this finger; by union regulations he is allowed to do no other work, not even to use a brush.

If a stenographer suffers a slight abrasion on the hand from the corner of the desk, the injury is not disabling and hence not compensable. If, however, the plant nurse applies a sulfonamide and the hand becomes swollen so that the patient is unable to type, she is entitled to compensation. If on a warm summer day, with her employer's permission, she eats lunch on the premises of the plant and suffers on her legs a dermatitis from poison ivy, or if she takes a short cut through the plant grounds and suffers intense swelling of the legs so that she cannot get to work, she is entitled to compensation. The same situation in a neighboring field, however, is not recognized as arising out of or in the course of employment and is therefore not compensable. The eruption on the fingers of a soda-fountain clerk is not totally disabling, because she can be put on dry work and treated without loss of time.

The disability from a true occupational dermatitis is never permanent, except for hypersensitivity, because all such dermatitides are curable. It has been ruled by the Massachusetts Supreme Court that sensitivity is not compensable; the worker must seek other work.

A disfiguring scar or a repulsive chloracne of the face lessens the worker's earning capacity in the labor market, and he should therefore be compensated, irrespective of his ability to work. In the Fennell case the employe sustained an injury to the left eye resulting in total loss of vision in that eye, and in such a change in appearance from the right eye that in turning the left eye its abnormal condition was apparent. Despite his testimony that he could do his work better after the accident because he was more careful, he was awarded compensation. The Industrial Accident Board concluded that total inability to do work and total in-

capacity to earn wages for work done are not synonymous, and that total incapacity is present if the employe in the case at bar, on account of the appearance of his eye, is unable to obtain work. Compensation is allowable when there is an impairment of earning capacity. When an employe is disabled from doing some kinds of work and is unable to obtain work of the type he is able to do, a finding of total incapacity is warranted (*Sullivan* 218 Massachusetts 141). On principle, when a worker is unable to obtain other employment because of visible, physical results of an industrial accident, his earning capacity is as much impaired as if he were physically disabled to the extent that he could do no work (Fennell 289 Massachusetts 89, 1935).

Statutes in many other states provide payment for disfigurement, without evidence that it results in loss of earning capacity, but in a few states, including Massachusetts, there is no such provision, and only when it interferes with earning capacity can disfigurement be made the basis of an award. In *Sweeting* v. *American Knife Company* (226 New York 199, 1919), in which an explosion disfigured the employe's nose and face, the New York court held that "serious facial disfigurement has a tendency to impair the earning power of its victims," although in New York payment is provided, by statute, for disfigurement. Courts and industrial accident boards recognize the difficulty encountered by the maimed, crippled or disfigured employe. An actress or waitress left with repulsive scars, preventing her from obtaining employment, has lost her earning capacity as much as if she were actually bedridden. As a matter of fact, the Pennsylvania Court, in *Naughton* v. *Kettl* (154 Pennsylvania Superior Court 318, 1944) and in *Eckley* v. *Rae* (128 Pennsylvania Superior Court 577, 1937), followed this theory, and in the latter case stated specifically, "It is a matter of common knowledge that there is a general disinclination on the part of employers to give work to cripples."

Bear[8] cites a case tried before the Industrial Accident Board, that of *Lillie Hendricks* v. *Chesterfield Laundry Service Company*. This employee was a thirty-one-year-old Negress who was operating a laundry pressing machine. A part of the machine weighing about 50 pounds shut down on her right forearm, burning her. She managed to free herself and then fainted. In treatment, a dye that formed a firm eschar over the wound was used. It slowly loosened around the edges, and for a time a new dye was applied to the raw areas. As the coagulum was gradually removed ointment was applied, until finally a granulating surface was obtained. The large open surface was then filled in with skin grafting. This graft took fairly well, except that where it crossed the wrist joint there was some stiffness and cracking due to the motion of the joint at that point. The important feature of the case, however, was that the patient was left with an extensive keloid formation, which disfigured her arm. The employe testified at the hearing that she was sent from an employment agency to two different families to do housework. The prospective employers kept looking at her arm, and the agency was notified after each interview that she had not been hired because the scar was considered obnoxious. The Commissioner found that this constituted a disability and awarded compensation, which the insurer paid without appeal to the courts.

## Treatment

Treatment of occupational dermatoses begins with the elimination of the causative factor. The ideal method is that of prevention, achieved in the first place by not allowing a potential hazard in the industrial process. Such elimination will never be possible in industry, however, because there will always be essential chemicals that affect a certain number of workers. These possible irritants or sensitizers should be properly labeled so that due precaution against harmful reactions can be taken. Education of the worker regarding care in handling such substances and the installation of facilities for the proper method of cleansing the skin after work are invaluable. Many workers have sustained eruptions from using gasoline, thinner, turpentine or harsh soaps on the skin to remove the day's grime. Supervision is necessary, because workers are apt to refuse to work with gloves or will take unnecessary short cuts in their work, and carelessness causes considerable trouble. A chemist was seen who extracted cashew-nut-shell oil, a notorious primary irritant and sensitizer. During the process of extraction he was careful, wearing a mask, protective clothing and gauntlet rubber gloves, but when the extraction was completed he thoughtlessly discarded them and washed the utensils with his bare hands. with a resulting dermatitis.

Early and correct diagnosis of an occupational eruption is most important. If the exact causative factor is easily recognized, removal of the hazard or protection of the worker from any possible contact, together with soothing applications, may be sufficient to prevent disability. If the worker is new on the job an attempt should be made to keep him on it, for if he can survive the first few weeks he may become more or less immune, as many have done. Such workers should be kept under close observation and removed from the work if the eruption spreads.

Twenty-five years of practice in industrial dermatology has produced experience that frequently clashes with papers and books on the subject of returning to work. Records in my office on industrial patients observed over a period of twenty years show that about 50 per cent returned to their old jobs. By exercising due care they were able to work for periods ranging from one to five years without a new attack, and the new attack fre-

quently followed an illness or a vacation. One baker has lost no time despite periodic attacks of baker's eczema for over ten years. His sensitivities have varied, at one time being due to the improver, at another to cinnamon and later to a combination of salt and lard. At times the face, hands and arms have been involved, but the eruption has never spread to other parts of the body. Other patients who previously presented occupational dermatoses have returned to my office with other forms of eruption, such as sensitization due to medication used in the treatment of trivial injuries, or secondary infection following a slight break in the skin.

Many occupational dermatoses arise not from the occupational exposure alone but from a combination of factors; examples of such patients are the man who paints at work and also at home, and the waitress who works all day and then does her housework. Many occupational dermatoses would not occur but for some intervening factor such as those just mentioned, intercurrent illness and internal medication, excessive fatigue or neglected injuries to the skin. These lower the threshold of resistance, and when the patient is relieved and these factors have been eliminated, the threshold rises and many workers can resume their work with impunity.

Anderson[9] elaborates on a suggestion made several years ago: the use of mild soothing solutions with a slight increase in the reaction in the presence of acids and a decrease in the presence of alkalies.[10] He states that four different points of attack can be applied to the problem of chemical neutralization of a cutaneous irritant. In the first place, direct chemical neutralization may be used; a corrosive and irritant alkali can be neutralized by a weak acid, such as acetic acid (vinegar) or citric acid (lemon juice). The same principle is involved in the use of weak alkalies in the neutralization of irritant acids. Secondly, one may detoxify the chemical irritant by another chemical, which reacts to form an insoluble or nonirritating compound. Thus, chromium compounds can be oxidized into innocuous metallic salts by sodium sulfite. Thirdly, the chemical phenomenon of absorption may be employed. Medications based on this phenomenon are the absorbent powders, such as charcoal and kaolin. Finally, the unusual emulsifying and detergent properties of the new synthetic wetting agents may be used to remove toxic chemicals from the skin. These suggestions are valuable if the causative factor is recognized immediately and the proper treatment is instituted. If a neutralizing solution is not available, plenty of water will dilute the irritant.

Wet dressings should be the first topical remedy. A 5 per cent solution of sodium hyposulfite, either hot or cold, is used in the treatment of poisoning from dyes and chromates. Wet dressings of physiologic saline solution are soothing. When there is only redness and swelling, a saturated solution of magnesium sulfate will produce quick results. When the skin is red, swollen and vesicular, a 5 per cent solution of aluminum acetate or 2 per cent solution of boric acid, either separately or combined, is extremely valuable, antipruritic and cooling and permits proper drainage. These dressings should be composed of heavy gauze or strips of Turkish toweling that have been boiled. They should be changed frequently to remove the debris and allow evaporation. Wet dressings of boric acid, citric acid or citrates may be applied to the so-called "cyanide rash" occasionally seen in jewelers. In the acute stages of cutting-oil folliculitis, the use of wet dressings of 25 per cent isopropyl alcohol has been beneficial. Potassium permanganate in a 1:4500 solution and 0.125 to 0.25 per cent of silver nitrate may be employed when there is secondary infection. Boiled milk (four parts) and lime water (one part) are soothing in cases of dermatitis about the orbits and sides of the neck, such as occurs from exposure to irritating dusts, fumes and resins.

Powders cool and dry the skin, and while protecting it from external irritation permit heat radiation. The combination of alternate wet dressings and dusting of the surface with powder quickly relieves the congestion. The mineral powders are better than the vegetable. The former — kaolin, bismuth compounds, magnesium and calcium carbonates, zinc oxide and zinc stearate — are absorptive and clean and are valuable when there is considerable weeping. Vegetable powders should be used only in combination with mineral powder, because of their tendency to swell and decompose. Wet dressings alone should not be applied for more than twenty-four to forty-eight hours, because they cause maceration. The combination of wet dressings and powders should not be employed for more than seventy-two hours.

If powders are used too long, they tend to cake and to interfere with secretions so that reactions of hypersensitivity or autosensitization appear, or they predispose to pyogenic infection, with the formation of intrafollicular pustules or lymphangitis.

If there is no marked redness or swelling, lotions may be applied immediately or within twenty-four hours. For a universal standby, Calamine Lotion (*National Formulary*), with 1 per cent phenol, is useful, but the physician should not limit himself to a single prescription, for as each eruption and skin varies, so should the local application. Properly prescribed and applied, lotions produce the best results and testify to the therapeutic skill of the physician, the pharmaceutical ability of the chemist and the training of the nursing attendant. Careful directions should accompany the prescription. Being a suspension of powder in fluid, it should be shaken well and spread or evenly sprayed over the skin. A soft paint brush or spray gun is advantageous when the surface is extensive. Glycerin is valuable because of its power to absorb moisture, but it retains the moisture and therefore should be

omitted in cold weather, because it makes the skin feel cold and sticky. I have used the formulas* referred to below in the treatment of various occupational dermatoses. When there is considerable secretion and danger of infection from the nature of the work (such as sensitization from soluble cutting oils), the following formula is useful:

| Substance | Amount |
|---|---|
| Calamine | 20 gm. |
| Zinc oxide | 20 gm. |
| Boric acid | 10 gm. |
| Glycerin | 5 cc. |
| Bentonite | 2 gm. |
| Lime water (as needed) to make a solution of | 250 cc. |

Bentonite is a colloidal clay that acts as a medium for suspending the powders in the liquid by producing a gel. For the erythematous, squamous eruption, such as that seen after contact with irritating dusts, fumes or resins, the following may be used:

| Substance | Amount |
|---|---|
| Phenol | 2 gm. |
| Zinc oxide | 30 gm. |
| Calamine | 30 gm. |
| Starch | 30 gm. |
| Glycerin | 30 cc. |
| Distilled water (as needed) to make a solution of | 250 cc. |

When there is marked pruritus, additional antipruritics may be added, such as the following:

| Substance | Amount |
|---|---|
| Menthol | 0.6 gm. |
| Phenol | 1.2 gm. |
| Solution of coal tar | 8.0 cc. |
| Calamine lotion (*N. F.*, as needed) to make a solution of | 250.0 cc. |

Coal-tar solution is much more satisfactory for the preparation of lotions and liniments if made with 70 per cent alcohol instead of 95 per cent. The addition of the cuticolored neocalamine in sufficient amount to match the patient's skin makes a more pleasing preparation. Neocalamine, however, stains clothing and bed linen. For the relief of an intensely itchy follicular eruption, seen after contact with rubber or mica, when there is no evidence of infection, the following lotions are valuable:

| Substance | Amount |
|---|---|
| Menthol | 0.6 gm. |
| Phenol | 1.2 gm. |
| Solution of coal tar | 10.0 cc. |
| Zinc oxide | 20.0 gm. |
| Talc | 20.0 gm. |
| Glycerin | 15.0 cc. |
| Alcohol (35 per cent, as needed) to make a solution of | 250.0 cc. |

| | |
|---|---|
| Menthol | 0.5 gm. |
| Solution of coal tar | 15.0 cc. |
| Glycerin | 10.0 cc. |
| Witch hazel | 100.0 cc. |
| Solution of boric acid (as needed) to make a solution of | 240 0 cc. |

| | |
|---|---|
| Solution of coal tar | 2.0 cc. |
| Phenol | 2.0 gm. |
| Menthol | 0.3 gm. |
| Boric acid | 3.5 gm. |
| Witch hazel | 100.0 cc. |
| Alcohol (70 per cent, as needed) to make a solution of | 250.0 cc. |

Isopropyl alcohol, being much less expensive, can be substituted for the alcohol.

The following is an old reliable prescription for dry, chapped hands and fingers:

| Substance | Amount |
|---|---|
| Tincture of benzoin | 15 cc. |
| Glycerin | 10 cc. |
| Rose water (as needed) to make a solution of | 250 cc. |

When the lips become chapped and fissured, bathing with the following is beneficial.

| Substance | Amount |
|---|---|
| Sodium borate | 6 gm. |
| Tincture of myrrh | 20 cc |
| Water (as needed) to make a solution of | 250 cc. |

When the skin becomes crusted, it should be bathed with equal parts of a 2 per cent solution of boric acid and a 10 per cent solution of aluminum acetate until the crusts soften and become detached. They should not be removed forcibly. Pastes are then indicated, the acute inflammation having subsided. Their action is more prolonged and protective, and they adhere to and soften the scales and crusts.[11] A paste is a rather stiff preparation consisting of powders and the vehicle, which may be glycerin, hydrocarbons, paraffin, petrolatum or animal or vegetable fats. Those containing glycerin are watery pastes, such as the following:

| Substance | Amount |
|---|---|
| Starch | 12 gm. |
| Distilled water | 24 cc. |
| Glycerin (as needed) to make a solution of | 120 cc. |

| | |
|---|---|
| Zinc oxide | 30 gm. |
| Talc | 30 gm. |
| Glycerin | 30 cc. |
| Distilled water | 30 cc. |

The most popular pastes are those having a base of petrolatum, such as the official paste of zinc oxide, containing equal parts of zinc oxide and powdered starch and 50 per cent of fat. On hairy surfaces, zinc oxide is apt to cause a folliculitis, in which event its proportion should be reduced. The following formulas are suggested:

| Substance | Amount |
|---|---|
| Zinc oxide | 2 gm. |
| Starch | 13 gm. |
| Petrolatum | 15 gm. |

| | |
|---|---|
| Solution of aluminum acetate | 10 cc. |
| Lanolin | 20 gm. |
| Zinc oxide paste | 30 gm. |

*Many of these formulas were developed with the collaboration of Leslie M. Ohmart and Mitchell J. Stoklosa, of the Department of Pharmacy, Massachusetts College of Pharmacy, Boston.

If itching persists in this subacute stage, one of the antipruritic lotions should be applied before the paste.

To avoid the necessity of two topical applications, a mixture of lotion and oil — that is, a liniment or emulsion — is used. Calamine Liniment (*National Formulary VII*) and Neocalamine Liniment (*National Formulary VII*) are excellent examples:

| Substance | Amount |
|---|---|
| Prepared calamine | 15 gm. |
| Zinc oxide | 15 gm. |
| Olive oil | 125 cc. |
| Solution of calcium hydroxide (as needed) to make a solution of | 250 cc. |
| Prepared neocalamine | 30 gm. |
| Olive oil | 100 cc. |
| Solution of calcium hydroxide (as needed) to make a solution of | 250 cc. |

Mineral oil may be substituted in the above prescriptions if, as sometimes happens, the patient is hypersensitive to olive oil or because of its shortage or expense. Various antipruritics can be added:

| Substance | Amount |
|---|---|
| Solution of coal tar | 8 cc. |
| Calamine liniment (*N. F. VII*, as needed) to make a solution of | 250 cc. |

If there is any evidence of pyogenic infection the following formula can be prescribed:

| Substance | Amount |
|---|---|
| Menthol | 0.5 gm. |
| Phenol | 1.0 gm. |
| Ichthammol | 7.5 gm. |
| Zinc oxide | 30.0 gm. |
| Olive oil | 100.0 cc. |
| Lime water (as needed) to make a solution of | 250.0 cc. |

In prescribing liniments other than those of the *National Formulary*, it is well to advise the pharmacist to use an electric mixer. Wetting agents, such as sodium lauryl sulfate, are valuable additions to liniments. Their effectiveness is based on their power to reduce surface tension between the solid and the solvent, thus permitting penetration and dispersion of the solid. The following formula is smooth and efficient:

| Substance | Amount |
|---|---|
| Zinc oxide | 15.0 gm. |
| Calamine | 15.0 gm. |
| Olive oil | 60.0 cc. |
| Sodium lauryl sulfate | 5.0 gm. |
| Phenol | 0.5 gm. |
| Water (as needed) to make a solution of | 250.0 cc. |

In persistent infiltrated extensive areas in which there is no evidence of infection, tar is useful, but it should be employed sparingly and only in the late stages. Liniments are of most benefit in an extensive eruption due to sensitization when the vesiculation has ceased, the crusts have become detached and the skin is red, dry and pruritic — that is, after the acute stage has subsided.

The majority of occupational dermatoses should be cured by the use of wet dressings, lotions and, finally, pastes and emulsions. Creams and ointments cause many of the complications of the treatment of occupational dermatoses. Ointments, especially, having no evaporating properties and being comparatively free from water, cause irritation and congestion when used in the initial stages. They may be employed in the subacute stage or in persistent eruptions. Neocalamine and Calamine Ointment (*National Formulary VII*) are excellent preparations. In fact, if physicians would prescribe more ointments of the *National Formulary*, they would have more expertly compounded prescriptions and less sensitization. When ointments contain drugs such as phenol, mercury, resorcin, Furacin and benzocain, the sulfonamides and penicillin, there is danger of absorption or sensitization. If there is no infection, there is no indication for their use. If secondary infection occurs, these drugs may be employed with caution and rarely for over one week, for by that time the infection should be relieved.

Ordinarily, an occupational dermatosis needs no internal therapy. When there is secondary infection, however, a sulfonamide or penicillin may be indicated. I prefer 50,000 units of penicillin in physiologic saline solution intramuscularly every three hours; it should be given no longer than five days, because that period is usually sufficient and sensitization is avoided. A dosage of 300,000 units of penicillin in wax and peanut oil daily is also useful, but the possibility of sensitization is increased by allergenic properties of the peanut oil. Benadryl and Pyribenzamine should be given during the period of injection. They have been helpful in controlling the spread and itching in the sensitization type of occupational dermatoses. If the patient is working, Benadryl should not be given because of its tendency to cause drowsiness. I prefer Pyribenzamine, which seemed to be of value in a few cases of industrial dermatitis. Autohemotherapy, alone or combined with previous intravenous injections of calcium gluconate, apparently helps when there is considerable edema or rapid extension of the eruption.

Some readers may criticize this array of formulas. Everyone knows that a normal skin may prefer one soap to another, usually owing to the difference in the reaction or to the amount of free alkali present, or a woman may try a dozen face powders before she finds one suitable to her skin. How much more important is topical application prescribed for the injured or traumatized skin! Frequently, a patient states that irritation or no relief resulted after the use of calamine lotion, but when she is persuaded to use the same lotion modified by the addition of boric acid, talc or starch or coal-tar solution, an immediately soothing response is obtained. A resourceful and successful therapist must have many topical applications at his com-

mand to obtain results in treating the various dermatoses. Expert knowledge of the medication and methods of using a few prescriptions is all that is necessary for the majority of cases, but it is the few that try one's patience and test one's therapeutic ability. With removal of the cause and with proper treatment and proper co-operation on the part of the patient, all industrial dermatoses can be cured.

* * *

Two and a half centuries after Ramazzini described the case of a young gilder who died from mercurial poisoning from inhalation, I saw a fatal case in a young woman — a pioneer worker in a new industry — who died from such exposure. That exposure has been eliminated after loss of a human life, which might have been prevented if the manufacturers had known of the danger of mercurial poisoning and had taken precautions against it.

Severe injuries have resulted from the use of x-rays in industry. Their use has been continued, but proper precautions are taken to prevent harmful effects. So, too, with the introduction of new processes as a result of the discovery of the atomic bomb. Today, practically all known elements can be made temporarily radioactive by means of the cyclotron. Proper medical supervision by industrial experts may prevent serious industrial dermatoses such as cancer of the skin, which is one of the aftermaths of excessive exposure to radiation.

The general practitioner cannot be expected to keep abreast of the rapid changes in industrial chemistry and physics, such as the radioactive substances. He must necessarily rely on industrial experts for information. With the vast amount of literature on medical therapy, however, he should know the indications and method of use of recent antibiotics and drugs.

## References


1. Downing, John G. Are patch tests of real value in dermatology? *New Eng. J. Med.* **219**:698-704, 1938.
2. Lane, C. G., et al. Industrial dermatoses: report by Committee on Industrial Dermatoses of Section on Dermatology and Syphilology of American Medical Association. *J. A. M. A.* **118**:613-615, 1942.
3. Downing, J. G. Dermatologist and Industrial Accident Board. *Indust. Med.* **14**:655-672, 1945.
4. Beaugrande. Recherches historiques et statistiques sur les maladies des ouvriers qui préparent les peaux en général. *Ann. d'hyg.* **18**: 241-280, 1862.
5. Osborne, E. D., and Hallett, Joseph J. Skin irritants. *New York State J. Med.* **42**:1529-1531, 1942.
6. O'Donovan, W. J. Psychological factor in dermatitis. *Brit. J. Dermat. & Syph.* **39**:49-54, 1927.
7. Hall, A. F. Occupational contact dermatitis among aircraft workers. *J. A. M. A.* **125**:179-185, 1944.
8. Bear, J. Personal communication.
9. Anderson, N. P. Neutralization as therapeutic principle in contact dermatitis. *Arch. Dermat. & Syph.* **49**:176-182, 1944.
10. Downing, J. G. Cutaneous eruptions among industrial workers: review of 2000 claims for compensation. *Arch. Dermat. & Syph.* **39**:12-32, 1939.
11. *Idem.* Treatment of common dermatoses. *M. Clin. North America* **29**:1095-1113, 1945.


# THE HEPATITIS OF HYPERTHERMIA

## Report of a Fatal Case


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PATIENTS receiving intensive artificial fever therapy occasionally develop jaundice. This phenomenon has recently been reported as a major complication of therapeutic hyperthermia by several different groups of observers.[1–3] In the reported series the incidence of jaundice has been as high as 19 per cent.[3]

The jaundiced patients follow a characteristic clinical course. Usually within the first twenty-four hours following fever, exaggerated nausea and vomiting occur. Within forty-eight hours the urine is dark and jaundice becomes apparent. There may be upper abdominal discomfort and tenderness over the liver. Fever, if present, is slight. In the great majority of cases the jaundice promptly disappears, usually within a week, and the patient rapidly recovers from the accompanying symptoms.

Although there is general agreement that the jaundice is the result of liver damage rather than of excessive blood destruction, divergent opinions have been expressed concerning the pathogenesis of the underlying hepatic disorder. The theory propounded by Brown et al.[4] — that inadequate replacement of salt and water is chiefly responsible for the jaundice — is widely held by those using artificial fever. MacDonald[3] suspected the sulfonamides, which are frequently administered simultaneously. More recently speculation has centered on the possibility of a virus etiology.

Descriptions of the histopathology of the liver could be found in only 2 cases, presumably because the syndrome is rarely fatal. Both descriptions are brief and lack illustrations. Wilbur and Stevens[5] reported their findings in a patient who received artificial fever therapy, developed jaundice and died on the third day after treatment; the liver weighed 2350 gm. and showed a diffuse early necrosis. Chunn and Kirkpatrick[6] described a similar case in which death occurred on the fourth day after fever and examination revealed a liver weighing only 1320 gm. and showing extensive atrophy.


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It is the purpose of this paper to report another series of hypertherm treatments in which jaundice appeared as a complication, to present the pathological findings in a fatal case and to discuss the evidence available concerning the pathogenesis of the condition. An understanding of the actual mechanism involved should lead to a reduction in its incidence.

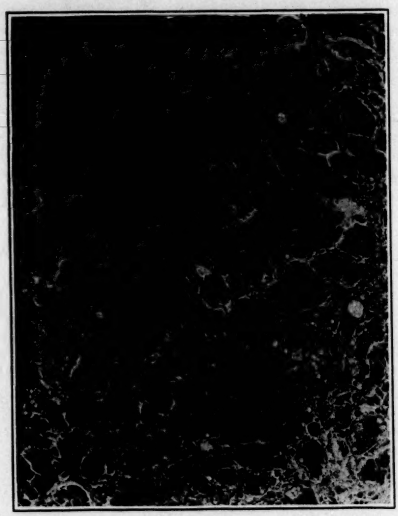

FIGURE 1. *Section of the Liver in a Case of Post-Hypertherm Hepatitis.*
*Death occurred on the fourteenth day of illness.*

During the early years of the war, all sulfonamide-resistant cases of gonorrhea among American forces in the Southwest Pacific were referred to a single Army general hospital for fever therapy. The methods employed in the treatment of these patients have already been reported by Harrison, Botsford and Ross.[7] Only men in good physical condition were subjected to this rather rigorous form of therapy. Each received 5 gm. of sulfathiazole over a period of eighteen hours prior to entering the cabinet. Heat was produced by ordinary incandescent lamps, and a high humidity was maintained. A treatment was considered satisfactory only when the rectal temperature could be maintained between 106 and 107°F. (41.1 to 41.5°C.) for seven hours. This degree and duration of fever were attained in a total of 524 treatments administered to 404 patients. All patients received physiologic saline solution by mouth and by vein during treatment. Sedatives were given to control restlessness. Oxygen was used when indicated.

Of the 404 patients so treated, 24 (6 per cent) developed clinical jaundice within a few days. In the great majority of cases the course of the disease differed in no way from that described above. One patient, however, developed severe liver damage and eventually died. This case was as follows:

Four hours after entering the cabinet the patient became excessively restless, and the rectal temperature suddenly rose to 108°F. (42.2°C.). He was immediately removed, unconscious and in a state of collapse. The skin was ashen gray and had ceased to sweat. The eyes wandered, and there were bilateral tonic movements of the extremities. Respirations were irregular and labored. The pulse was weak and rapid. The systolic pressure was low, and the diastolic was unobtainable. The body temperature was reduced as quickly as possible by means of intravenous fluids and ice packs. Within a few hours the patient regained consciousness, and on the following morning he was mentally alert with a normal temperature. There were no neurologic sequelae.

About 24 hours after removal from the cabinet, however, the patient became nauseated and vomited repeatedly. Within 48 hours a tender liver became palpable, and jaundice was apparent. During the ensuing week the liver shrank, but the jaundice deepened. Gross hematuria, oliguria, uremia and anasarca developed. Efforts directed at increasing the renal output included plasma and whole blood intravenously. In the 2nd week the patient began to show signs of improvement. The hematuria ceased, the urinary output increased considerably, the nonprotein nitrogen dropped, and he again became rational. Vomiting had persisted, however, and on the 14th day after fever therapy he had a massive and fatal hematemesis.

*Autopsy.** Post-mortem examination showed the body to be quite icteric, and there was considerable anasarca, with 2200 cc. of clear ascitic fluid. Areas of acute ulceration were present over the lower esophagus — a frequent finding in patients who have experienced prolonged nausea and vomiting. The terminal hemorrhage undoubtedly arose from one of these sites.

The liver weighed 1800 gm., representing slight enlargement. The capsule was smooth, and the parenchyma was yellow and friable.

Microscopical examination revealed that the normal lobular architecture was obscured by relatively acellular areas alternating with areas of regenerating liver cells (Fig. 1). The former consisted of collapsed edematous stroma containing only an occasional liver cell. These showed rather small pale nuclei, in many of which the cytoplasm was laden with fat and a variety of pigments. Interspersed between these degenerating liver cells were moderate numbers of macrophages containing similar pigments. In the areas of regeneration, which comprised over 70 per cent of the liver substance, the parenchymal cells lay in relatively unorganized masses. Although most bore an intimate relation to sinusoidal endothelium, many had failed to establish continuity with the biliary system. Intracellular and intracanalicular masses of bile pigment were prominent features. The regenerating cells characteristically contained abundant cytoplasm, which frequently assumed bizarre shapes. Many contained more than one nucleus. Occasional cells showed intranuclear and intracytoplasmic inclusion bodies. These were spherical, hyaline, eosinophilic masses. Those that were intranuclear were separated from the ring of condensed nuclear chromatin by a clear zone (Fig. 2). In the portal areas there was active proliferation of the bile capillaries. Some of these areas were moderately infiltrated with lymphocytes and an occasional polymorphonuclear leukocyte. There was perhaps slight fibroblastic proliferation but no increase in collagen. The vessels showed no significant lesions. Had the fatal hemorrhage not intervened, it is probable that the liver would have returned to normal function.

The combined weight of the kidneys was 665 gm., which is about twice the normal weight. Both were essentially

*Army Institute of Pathology, No. 130943.

similar. The capsules were smooth. The parenchyma was pale and bulging with edema. The renal pelves, as well as the remainder of the genitourinary system, were not abnormal.

Microscopically, in addition to marked interstitial edema and an occasional small hemorrhage, there was precipitated protein throughout all portions of each nephron (Fig. 3). The outstanding abnormalities were observed in the distal convoluted and collecting tubules, many of which showed necrosis and varying stages of regeneration. The latter process predominated. Many of these tubules contained

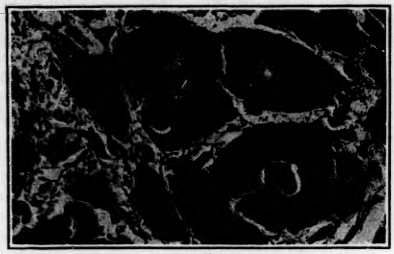

FIGURE 2. *Intranuclear Inclusion Body in Liver Cell.*

intraluminal masses of red-brown material — so-called "pigment casts." In places these were surrounded by polymorphonuclear and histiocytic phagocytes. A few tubular cells contained intracytoplasmic droplets of yellow-green material resembling bile pigment. No inclusion bodies were found.

There was some edema of the lungs and brain but no other significant abnormality.

The findings in the kidneys were identical with those described by Lucké[8] as characteristic of "lower nephron nephrosis," a clinical and pathological syndrome that may complicate a variety of medical and surgical conditions. The syndrome frequently follows transfusion incompatibilities,[9] but in the case presented above, manifestations of renal damage preceded transfusion. The syndrome may also follow intravascular hemolysis in malaria,[10] severe burns[11] and sulfonamide-sensitive states.[12] The patient described above did not have malaria, nor was he burned. Other evidence of sulfonamide sensitivity was lacking. Necrosis of the lower nephron and the presence of pigment casts have also been described in a variety of liver diseases. Under such circumstances the renal pathology is usually referred to as cholemic or "bile" nephrosis. In the present case it seems likely that the renal lesions were secondary to the severe liver damage.

In that event the findings in the liver are not pathognomonic of any specific condition. They are, however, inconsistent with the lesions produced by sulfonamide sensitivity.[12] Except for the occasional case in which sensitivity develops, evidence of a hepatotoxic action on the part of any of the sulfonamides is highly questionable, a point emphasized in two recent reviews of the subject.[13, 14] That the sulfonamides play no part in the production of post-hypertherm hepatitis was demonstrated by Wallace and Bushby,[15] who showed that the incidence of jaundice was no greater among patients simultaneously receiving sulfonamides than among those not receiving them.

The possibility that the hepatitis of hyperthermia is of virus origin has occurred to several observers. Such a concept presupposes the presence of a hepatotoxic agent latent in the body and in some way activated by the treatment. Fever therapy was repeated in 2 of MacDonald's[3] jaundiced patients and in 1 of our own. In no case did clinical jaundice reappear after the second treatment.

The virus of herpes simplex is harbored by many people, and when the proper stimulus — including heat — is forthcoming, clinical herpes appears. Herpes labialis has always been a common complication of artificial fever therapy. It occurred in 66 per cent of our own cases. Although the intranuclear inclusions found in the liver in the case presented above are indistinguishable from those found in herpes simplex infections, this does not imply a herpetic or even a virus etiology for the

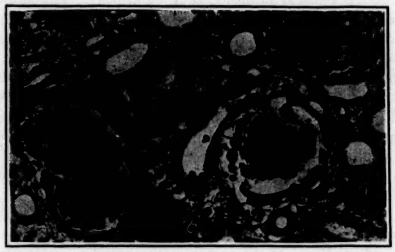

FIGURE 3. *Section of a Kidney, Showing Damage to Tubular Epithelium and Pigment Casts.*

hepatitis. Inclusion bodies of one sort or another have been described and produced in a great variety of nonvirus conditions. Inclusions indistinguishable from those of yellow fever, for example, have been observed in liver cells of burned patients treated with tannic acid.[16] Furthermore, the virus of herpes is not known to infect the liver of man or animal.

The patient, like all military personnel in the theater, had previously received attenuated yellow-fever-virus vaccine. At the time the fever treatments were being given, hepatitis was fairly prevalent among the troops. Whether "epidemic" and "serum" hepatitis are in reality the same disease has not yet been established. It has been amply demonstrated, however, that the serums of certain

persons at times harbor a hepatotoxic virus. Whether it can be activated by fever is at the moment unknown. Morphologically, except for the presence of inclusion bodies, the liver in the case discussed above bears many similarities to the pathology of infectious hepatitis described by Lucké[17] and many others. From a clinical point of view, however, the hepatitis that follows fever therapy is as a rule less severe and of considerably shorter duration than the infectious hepatitides.

A more probable etiology for this form of hepatitis is to be found in high body temperatures per se. Although the critical temperature above which liver cells become irreversibly damaged is unknown and probably varies to a certain extent with the state of nutrition of the individual cells, there is evidence that this point is not far above those frequently encountered. King et al.[2] showed that the incidence of jaundice among patients receiving fever therapy was higher in a group whose temperatures were maintained at 106.6°F. than in a group held at 106.0. More significantly, they noted that jaundice was particularly likely to occur if the temperature were allowed to rise for even brief periods above the former figure. Evidence also exists that the majority of patients receiving intensive fever therapy suffer some degree of liver damage, even though clinical jaundice fails to appear. The same authors showed that in a group of 40 consecutive cases a subclinical rise in serum bilirubin occurred in 75 per cent. Hippuric acid tests performed before treatment and repeated three days later showed a significant reduction in liver function in 12 cases. Wilson and Doan[18] studied a similar group of patients and found a post-therapeutic rise in bilirubin and an increased retention of bromsulfalein in each case; the degree and duration of fever were not recorded.

Although observations on animals subjected to experimental hyperpyrexia include no clinical or pathological effects exactly comparable to post-hypertherm hepatitis in man, changes in the liver have frequently been described. Hartman and Major[19] placed dogs in a Kettering hypertherm cabinet and maintained their rectal temperatures between 107 and 110°F. (41.7 and 43.3°C.) for five to seven hours. The animals died or were sacrificed at intervals from one to seventy-two hours later. The predominant lesions were those of congestion and hemorrhage, but many livers showed extensive midzonal necrosis. Hall and Wakefield[20] maintained dogs at comparable temperatures by similar means. Lesions in the liver were limited to cloudy swelling, probably because the animals were examined too soon after exposure for more significant morphologic changes to have developed. Other investigators have raised the temperatures of animals by less pertinent means. Jacobsen and Hosoi,[21] using high-frequency currents, maintained dogs for periods up to twelve hours with rectal temperatures of 108 to 111°F. (42.2 to 44.0°C.). Most of the dogs died promptly, but some of the survivors showed focal necroses in the liver.

Rawlinson and Kellaway[22] perfused cat livers with hot saline solutions and determined in the perfusate the concentrations of several cellular constituents. Their results indicate that liver cells are severely damaged by temperatures as low as 104°F. (40°C.) when maintained for six hours. Although the conditions of perfusion produced cellular damage, that which occurred at high temperatures was significantly greater than could be accounted for by a simple exponential increase in the rate of processes operating at body temperature.

Opportunity for studying the morphologic effects of high temperatures on the human liver does not occur often because hyperpyrexia usually brings death within a few hours or the patient survives. In prompt deaths signs of cerebral damage dominate the clinical and pathological picture. The liver may show "cloudy swelling." Occasionally, however, the survival period is adequate for clinical signs of liver failure and for morphologic manifestations of necrosis to develop. Wilbur and Stevens[5] described a patient who lived for three days after a sunstroke during which the temperature had reached 110°F. (43.3°C.). Jaundice was present, and there was definite evidence of necrosis in the liver. Malamud, Haymaker and Custer[23] recently studied the pathology in 125 fatal cases of heatstroke among American troops. They found frank necrosis of the liver in only 12 cases, but all these occurred in patients who had survived for more than thirty hours, whereas the majority had died in less than twenty-four hours. Jaundice appeared clinically in some of the former group.

It is a common biologic observation that unicellular organisms differ widely in their sensitivity to heat, the critical temperature being, within limits, specific for the species. Among multicellular organisms certain highly differentiated cells are more sensitive to heat than less differentiated ones. In man there is evidence that hepatic cells, along with certain cells of the central nervous system, are among the first to be damaged by high temperatures. Although the part played by oxygen deficiency may be an intimate one, destruction of essential enzyme systems appears a more probable mechanism.

## Summary

Hepatitis, with or without jaundice, frequently complicates artificial fever therapy. Liver damage also occurs after other forms of hyperpyrexia.

The pathological findings in a fatal case of post-hypertherm hepatitis are presented. The liver showed extensive necrosis followed by regeneration.

Available evidence indicates that liver cells, in addition to certain cells of the nervous system, are particularly susceptible to damage by high fever.

## References

1. Warren, S. L., Scott, W. W., and Carpenter, C. M. Artificially induced fever for treatment of gonococcic infections in male. *J. A. M. A.* **109**:1430-1434, 1937.
2. King, A. J., Williams, D. I., and Nicol, C. S. Hyperthermia in treatment of resistant gonococcal and non-specific urethritis. *Brit. J. Ven. Dis.* **19**:141-154, 1943.
3. MacDonald, R. M. Toxic hepatitis in fever therapy. *Canad. M.A. J.* **51**:445-449, 1944.
4. Brown, H. R., Jr., Clark, W. F., Jones, N., Walther, J., and Warren, S. L. Relationship of dehydration and overhydration of blood plasma to collapse in management of artificial fever therapy. *J. Clin. Investigation* **22**:471-485, 1943.
5. Wilbur, E. L., and Stevens, J. B. Morbid anatomic changes following artificial fever, with report of autopsies. *South. M. J.* **30**:286-290, 1937.
6. Chunn, G. D., and Kirkpatrick, C. L. Fatal result of artificial fever therapy: case report. *Mil. Surgeon* **81**:281-287, 1937.
7. Harrison, J. H., Botsford, T. W., and Ross, F. P. Treatment of resistant gonorrhea with induced hyperthermia supplemented by sulfonamide therapy. *J. Urol.* **51**:215-227, 1944.
8. Lucké, B. Lower nephron nephrosis: renal lesions of crush syndrome, of burns, transfusions, and other conditions affecting lower segments of nephrons. *Mil. Surgeon* **99**:371-396, 1946.
9. Ayer, G. D., and Gauld, A. G. Uremia following blood transfusion: nature and significance of renal changes. *Arch. Path.* **33**:513-532, 1942.
10. Foy, H., Altmann, A., Barnes, H. D., and Kondi, A. Anuria, with special reference to renal failure in blackwater fever, incompatible transfusions, and crush injuries. *Tr. Roy. Soc. Trop. Med. & Hyg.* **36**:197-238, 1943.
11. Goodpastor, W. E., Levenson, S. M., Tagnon, H. J., Lund, C. C., and Taylor, F. H. L. Clinical and pathologic study of kidney in patients with thermal burns. *Surg., Gynec. & Obst.* **82**:652-670, 1946.
12. French, A. J. Hypersensitivity in pathogenesis of histopathologic changes associated with sulfonamide chemotherapy. *Am. J. Path.* **22**:679-702, 1946.
13. Jones, C. M. Liver intoxication. *New Eng. J. Med.* **230**:766-774, 1944.
14. Ottenberg, R., and Spiegel, R. Present status of non-obstructive jaundice due to infectious and chemical agents: causative agents, pathogenesis, inter-relationships, clinical characteristics. *Medicine* **22**:27-71, 1943.
15. Wallace, J., and Bushby, S. R. M. Hazards of hyperthermic treatment. *Lancet* **2**:459-464, 1944.
16. Duffin, J. D. Liver necrosis following burns. *Canad. M. A. J.* **47**: 138, 1942.
17. Lucké, B. Pathology of fatal epidemic hepatitis. *Am. J. Path.* **20**: 471-593, 1944.
18. Wilson, S. J., and Doan, C. A. Pathogenesis of hemorrhage in artificially induced fever. *Proc. Soc. Exper. Biol. & Med.* **41**:115-117, 1939.
19. Hartman, F. W., and Major, R. C. Pathological changes resulting from accurately controlled artificial fever. *Am. J. Clin. Path.* **5**: 392-410, 1935.
20. Hall, W. W., and Wakefield, E. G. Study of experimental heat stroke. *J. A. M. A.* **89**:177-182, 1927.
21. Jacobsen, V. C., and Hosoi, K. Morphologic changes in animal tissues due to heating by ultrahigh frequency oscillator. *Arch. Path.* **11**:744-759, 1931.
22. Rawlinson, W. A., and Kellaway, C. H. Studies on tissue injury by heat: liberation of enzymes from perfused liver. *Australian J. Exper. Biol. & M. Sc.* **22**:69-81, 1944.
23. Malamud, N., Haymaker, W., and Custer, R. P. Heat stroke: clinico-pathologic study of 125 fatal cases. *Mil. Surgeon* **99**:397-449, 1946.


# SYPHILITIC PRIMARY OPTIC ATROPHY*

## A Review of 54 Cases


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BOSTON


A FEW years ago the outlook regarding vision for patients with syphilitic primary optic atrophy was generally considered extremely poor, regardless of the type of therapy used. This attitude tends to persist in spite of the gratifying reports by Moore et al.[1] and others[2, 3] of unusually successful results with malaria treatment. One of the reasons for pessimism is that there is too often an excessive delay in starting treatment and that, as a result, optic atrophy may progress to blindness before adequate treatment is instituted. This delay often appears to be due to failure to make the proper diagnosis, lack of appreciation of the potential rapidity of progress of the disease or confusion regarding what constitutes adequate or proper therapy.

In view of these considerations we have undertaken to report an analysis of our cases of syphilitic primary optic atrophy.

### Material

A series of 54 patients with syphilitic primary optic atrophy admitted to the Boston Psychopathic Hospital during the years 1921 to 1944 formed the basis of the investigation. The case records were reviewed and analyzed from the point of view of history, clinical findings and response of vision to treatment.

The ages ranged from nineteen to sixty-two years. The age-distribution curve was essentially the same as that for patients with neurosyphilis in general, the maximum number of cases occurring between the ages of forty and fifty.

Of the 54 patients, 51 were males and 3 were females. There were only 2 Negroes in the series.

The duration from the occurrence of the primary syphilitic lesion to the onset of the visual loss (as judged by data available in only 20 cases) varied from ten to thirty-three years, with an average of twenty years.

### First Manifestations of Neurosyphilis

The first clinical manifestations of neurosyphilis in cases that later developed optic atrophy were as follows:

| Symptom | No. of Cases |
|---|---|
| Gradual loss of vision | 34 |
| Lightning pains | 3 |
| Personality change | 3 |
| Difficulty in concentration or memory | 3 |
| Gastric crises | 2 |
| Pain in eyes | 2 |
| Diplopia | 2 |
| Ptosis | 1 |
| Numbness on right side of face | 1 |
| Dysarthria | 1 |
| Urinary incontinence | 1 |
| Aphasia | 1 |
| Total | 54 |

It is interesting that in 34 cases (63 per cent) the first manifestation was gradual loss of vision. It

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is therefore apparent that every patient with the complaint of gradual loss of vision should have adequate investigation for central-nervous-system syphilis, even when other signs are absent.

### Serologic Findings

In all but 1 case there was a report of the admission blood Wassermann or Hinton test, or both. In 39 cases blood Hinton tests were positive in 38 and doubtful in 1. In 19 cases blood Wassermann tests were positive in 13, doubtful in 2 and negative in 4. From these data it is apparent that a negative blood Hinton or Wassermann test is rare in untreated or inadequately treated cases of syphilitic primary optic atrophy.

### Pupillary Abnormalities

Of 51 cases in which the pupillary findings were recorded on admission, 49 showed pupillary abnormalities characteristic of neurosyphilis. Thirty-six patients were recorded as having Argyll–Robertson pupils, and 13 as having irregularity, inequality of the size of the pupils or absent light reaction.

### Diagnosis on Admission

After careful study of the case records, the following diagnoses were made: syphilitic primary optic atrophy alone, 15 cases; syphilitic primary optic atrophy with tabes, 20 cases; syphilitic primary optic atrophy with general paresis, 14 cases; and syphilitic primary optic atrophy with taboparesis, 5 cases.

Table 1. *Degree of Tabetic Involvement in Cases with Tabetic Features.*

| Involvement | No. of Cases | No. of Cases with Lightning Pains | No. of Cases with Tabetic Bladder | No. of Cases with History of Gastric Crises |
|---|---|---|---|---|
| No ataxia; absence of tendon reflexes in lower extremities | 15 | 4 | 2 | 3 |
| Slight to moderate ataxia or positive Romberg sign | 10 | 6 | 1 | 0 |
| Marked ataxia | 0 | — | — | — |

In 19 cases there was a paretic element, whereas in 25 there was a tabetic element. Our experience that optic atrophy is found much more frequently in association with tabes than with general paresis coincides with the reports of others.[1] Optic atrophy occurs more commonly, however, in association with general paresis than may be generally appreciated.

An analysis of the degree of tabetic involvement in the 25 cases with tabetic features is presented in Table 1. It was observed that the tabetic picture was essentially one of a mild degree, none of the cases showing marked ataxia.

### Visual Fields

In general, the visual fields showed irregular constriction, which was usually of moderate degree even though visual acuity was markedly diminished These findings are in contrast to those in trypars-amide optic atrophy, in which marked constriction of the visual fields often occurs and is usually accompanied by only slight loss of central vision.

### Development of Blindness*

In 43 cases in which data were available, the onset of visual loss was bilateral in 11 and unilateral in 32. Of the latter group, 16 cases began with involvement of the right eye and 16 with involvement of the left eye. Cases with unilateral onset, if untreated, usually developed involvement of the second eye within a few months. In untreated cases, however, optic atrophy occasionally remained unilateral for longer periods, the maximum duration being three years.

Untreated cases showed widely differing rates of progression. In the most rapidly progressive case complete blindness developed bilaterally within twenty-two days. The patient with the slowest progress, after seven years without treatment, had visual acuity of 10/100 in one eye and blindness in the other. One of the notable trends was the rather frequent development of blindness in both eyes within a twelve-month period, emphasizing the need for intensive early treatment.

### Treatment before Onset

In this series treatment prior to the development of optic atrophy was inadequate, permitting the hypothesis that visual involvement might have been prevented had more active measures been used. Only 15 patients (28 per cent) received any treatment prior to the development of optic atrophy. In these cases, chemotherapy alone was employed, consisting usually of only a few arsenical and bismuth injections. No patient in the series received fever treatment before the onset of optic atrophy.

Ten patients who had been fortunate enough to receive chemotherapy were given this treatment two to twenty years before the development of any evidence of optic atrophy. Five patients, however, developed the first signs of optic atrophy while receiving a course of routine antisyphilitic treatment. Therefore, syphilitic optic atrophy may begin and progress in some persons even though active chemotherapeutic measures are being used. In other words, chemotherapy is no guarantee against the development of optic atrophy.

### Effect of Treatment

Of 43 patients who were not totally blind when treatment was started, 27 were followed for two years or longer after treatment had been instituted. The average duration of follow-up study in these cases was seven years.

Figure 1 shows the superiority of fever therapy as compared to chemotherapy in these cases. Of

*In this study an eye was considered blind if the visual acuity was 1/200 or less.

the 11 patients treated only with chemotherapy,* 6 (55 per cent) were blind on follow-up study of two years or longer. Of the 16 patients treated with fever therapy in addition to chemotherapy, only 2 (13 per cent) were blind on follow-up examination two years or more after treatment. In these 16 cases, fever therapy was usually followed by chemotherapy for one year or more. In 4 of the 16 cases, fever was artificially induced. The remaining 12 patients received malaria treatments, the number of chills varying from five to seventeen. The series of cases is too small to determine whether treatment with malaria was superior to treatment with artificial fever. It is interesting, however, that none of the 4 patients treated with artificial fever were found to be blind on follow-up study.

In general, the cases treated with chemotherapy had been of a less rapidly progressive variety prior to treatment than those chosen for fever therapy. It is also worth noting that in all 5 patients whose visual loss was arrested by means of chemotherapy alone, the optic atrophy was essentially unilateral; on follow-up study all were found to be blind in one eye but to have little or no visual loss in the other. Moore[1] has stressed the fact that patients in whom the atrophic process is still unilateral respond best to treatment. These 6 cases, therefore, comprised a selected group of patients who were most suitable for treatment and in whom chemotherapy alone was apparently sufficient to prevent blindness in the eye showing little or no involvement. One is not justified, however, in recommending chemotherapy alone for such cases because in similar cases treated with chemotherapy follow-up study revealed complete blindness in both eyes.

In the entire series there were only 2 cases in which vision improved after treatment, and in both, the treatment had consisted of intensive malaria therapy followed by chemotherapy. In 1 case, immediately prior to the onset of treatment, the patient was blind in the right eye and had 20/100 vision in the left; four years later visual acuity was found to be 20/200 in the right eye and 20/30 in the left. In the other case, immediately before treatment, the patient was blind in the left eye and had 20/40 vision in the right, but three months later visual acuity was found to be 20/200 in the left eye and 20/20 in the right. It is not to be expected, however, that therapy will improve vision but that, with good fortune, vision will not be further impaired.

### Cerebrospinal-Fluid Findings

The cerebrospinal-fluid findings were classified according to severity as Group I, II or III (the last being the strongest and equivalent to the so-called "paretic formula"), in accordance with the classification of Moore.[1] Analysis of the first cerebrospinal-fluid findings recorded after the onset of syphilitic primary optic atrophy revealed that 41 patients (76 per cent) had Group III fluids whereas 13 had Group II fluids. Of the latter, 11 patients (85 per cent) had received treatment during the interval between the onset of the optic atrophy and the examination of the fluid. Of the 41 patients with Group III fluids, however, only 19 (46 per cent) had received treatment during the interval between the onset of the optic atrophy and examination of the fluid. These findings indicate that, in general, syphilitic primary optic atrophy is accompanied by strongly positive cerebrospinal-fluid findings unless antisyphilitic treatment has been started.

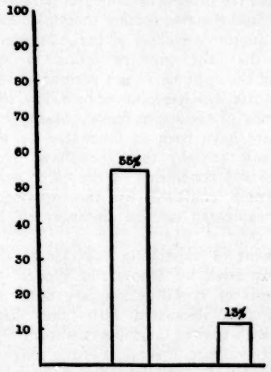


Figure 1. *Results of Treatment of Syphilitic Primary Optic Atrophy by Means of Chemotherapy, as Compared to Fever Therapy Combined with Chemotherapy, on Follow-up Study of Two Years or Longer.*

A further study was made of the cerebrospinal fluid in cases in which, as a result of treatment, optic atrophy had become definitely arrested for two years or longer (from two to fifteen years). There were 11 such cases, in 10 of which the cerebrospinal fluid had been examined during the six months following arrest of the optic atrophy. Only 1 of these patients had a Group III fluid, 3 a Group II fluid, 5 a Group I fluid and 1 a normal fluid. In the 9 cases with positive cerebrospinal-fluid findings the fluids later became negative with continued treatment (from nine months to about seven years). There was only 1 case in which visual loss was progressive after the cerebrospinal fluid had become negative. Since this patient was a diabetic, aged sixty years, the question whether the progression of visual loss was due to diabetic retinopathy rather than syphilitic primary optic atrophy remained unanswered.

The above data indicate that, in general, syphilitic primary optic atrophy becomes arrested before the cerebrospinal fluid becomes normal and that, when

*Four patients received intraspinal or intracisternal treatment in addition to routine chemotherapy.

the optic atrophy becomes arrested, the cerebrospinal-fluid findings usually fall in Group I or II.

## Discussion

One of the most striking findings was the high incidence of Group III cerebrospinal fluids (paretic formula) in cases of syphilitic primary optic atrophy, even though many of the patients had received some treatment before examination. These findings support the histologic studies of Bruetsch,[4] who states that "the pathologic basis of syphilitic optic atrophy is more like the process of dementia paralytica than of tabes," and remarks further that his findings uphold the anatomic studies of Leri,[5] Stargardt[6] and Richter[7] that the primary lesion in syphilitic atrophy of the optic nerve is a peripheral and interstitial neuritis, which is followed by a slow, secondary degeneration of the nerve fibers. Many writers on this subject have been so fascinated by the term tabetic optic atrophy that they have overlooked this important conclusion of the early workers or have become confused by the many different opinions expressed on the pathogenesis of optic atrophy.

This point of view is in contrast to that previously expressed by Moore and Woods[8] that the pathogenesis of syphilitic primary optic atrophy, which is often associated with tabes dorsalis, is identical with that of tabes dorsalis itself.

Indirect evidence in support of the conclusions of Bruetsch is found in the extensive perimetric studies of Sloan and Woods,[9] who observed that the lesion responsible for syphilitic atrophy of the optic nerve and visual-field defects lies in the optic nerves rather than in the chiasm or posterior to it and is probably a peripheral and interstitial neuritis associated with secondary degeneration of the nerve fibers.

In view of the strongly positive cerebrospinal-fluid findings in syphilitic primary optic atrophy one might anticipate that these patients would require at least as intensive treatment as patients with general paresis. This appears to be true, and since blindness may develop rapidly, it is our opinion that all these patients should receive the most intensive treatment available as early as possible in the course of the disease, in the hope of preventing further damage to diseased nerves and thereby of preserving useful vision. In a review of our cases it became apparent that several cases had progressed to complete blindness without treatment and that in many others intensive treatment had been delayed or lacking.

Our favorable results with malaria therapy support the findings of Moore,[1] who reported that of 32 patients receiving malaria therapy, only 14 per cent were blind at the end of two years.

Unfortunately, we had too few patients treated with artificial fever to be able to evaluate its effectiveness adequately. In the 4 cases treated, however, the results were satisfactory. When these cases are added to those of Menagh,[10] who obtained a satisfactory outcome in 4 of 6 cases so treated, Culler and Simpson,[11] who obtained satisfactory results in 13 of 16 cases, and Neymann and Osborne,[12] who obtained a satisfactory response in 4 of 6 cases, one is left with the impression that artificial fever is definitely effective in syphilitic primary optic atrophy.

## Summary

In 54 patients with syphilitic primary optic atrophy, seen at the Boston Psychopathic Hospital between 1921 and 1944, the first manifestation of neurosyphilis was usually gradual loss of vision.

Although syphilitic primary optic atrophy occurs most frequently in association with tabes, as a rule the tabetic features are mild.

Some abnormality of the pupils characteristic of neurosyphilis is almost always present.

A negative blood Wassermann or Hinton test is rare in untreated or inadequately treated cases.

Syphilitic primary optic atrophy is, in general, accompanied by a strongly abnormal cerebrospinal fluid (Group III) characteristic of the paretic formula. This finding is consistent with the studies of Bruetsch, in which the pathologic basis of this disorder was found to be more like the process of general paresis than that of tabes.

Syphilitic primary optic atrophy may respond well to fever therapy provided that treatment is started before useful vision is lost. Of 16 patients treated with artificial fever only 2 (13 per cent) were found to be blind on follow-up study of two years or longer. Although the available data are insufficient to determine whether artificial fever is as effective as malaria therapy, the former is definitely an important addition to the therapeutic armamentarium.

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## References

1. Moore, J. E., Hahn, R. D., Woods, A. C., and Sloan, L. L. Treatment of syphilitic primary optic atrophy. *Am. J. Syph., Gonor. & Ven. Dis.* **26**:407-473, 1942.
2. Clark, C. P. Rôle of malaria in control of atrophy of optic nerve due to syphilis: study of 12 cases. *Arch. Ophth.* **15**:250-269, 1936.
3. Dattner, B., Thomas, E. W., and Wexler, G. *The Management of Neurosyphilis.* 398 pp. New York: Grune & Stratton, Inc., 1944. P. 286.
4. Bruetsch, W. L. Malaria therapy in syphilitic primary optic atrophy. *J. A. M. A.* **130**:14-18, 1946.
5. Leri, A. Étude du nerf optique dans l'amaurose tabétique. *Nouv. iconog. de la Salpetrierre* **17**:358-375, 1904.
6. Stargardt. Über die Ursachen des Sehnervenschwundes bei der Tabes und der progressiven Paralyse. *Arch. f. Psychiat.* **51**:711-776, 1913.
7. Richter, H. Zur Histogenese der Tabes. *Zschr. f. d. ges. Neurol. u. Psychiat.* **67**:1-189, 1921.
8. Moore, J. E., and Woods, A. C. Pathology and pathogenesis of syphilitic primary optic atrophy: critical review. *Am. J. Ophth.* **23**: 1-40, 1940.
9. Sloan, L. L., and Woods, A. C. Perimetric studies in syphilitic optic neuropathies. *Arch. Ophth.* **20**:201-253, 1938.
10. Menagh, F. R. Treatment of syphilis with hyperpyrexia, with observations on prognosis of optic atrophy. *Am. J. Syph., Gonor. & Ven. Dis.* **21**:609-621, 1937.
11. Culler, A. M., and Simpson, W. M. Artificial fever therapy in cases of ocular syphilis. *Arch. Ophth.* **15**:624-644, 1936.
12. Neymann, C. A., and Osborne, S. L. Development of hyperpyrexia. *Arch. Phys. Therapy* **15**:149-155, 1934.

# INHIBITION OF CUTANEOUS PAIN RESPONSES BY THE LOCAL APPLICATION OF COLD*

## A Simple Method of Reducing the Pain of Hypodermic Injections

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THE increased use of antibiotic therapy as well as other medications and fluids administered by hypodermic injection has raised the question of the effectiveness and practicality of employing cold to relieve the pain of the repeated and often terrifying encounters with the needle experienced particularly by sick children. Inquiry revealed that hundreds of intramuscular and subcutaneous injections alone are performed every day at the Children's Hospital. Frequently, the mental and physical anguish associated with the numerous injections given to a critically ill patient is not inconsiderable.

It seemed desirable to determine first of all the physiologic relation between the temperature of the skin and the discharge of impulses from cutaneous pain receptors. That nerve conduction may be temporarily interrupted by temperatures that never reach the freezing point is well known. This has been demonstrated clinically by the effectiveness of refrigeration anesthesia in surgery of the extremities. It has also been measured in experimental animals. Denny-Brown and his co-workers[1] cooled the exposed sciatic nerve of cats with circulating brine. They found that when the temperature of the brine was 2°C. or higher and the temperature within the nerve itself 8 to 11.6°C. for as long as two hours, there was temporary interruption of function with no evidence of any permanent damage to the nerve. Gasser[2] studied the effect of temperature changes on nerve conduction in the frog. He found that cooling a nerve caused its action potential to decrease in a characteristic way. On cooling from 30 to 20°C., the action potential fell off slowly. The rate of fall then progressively increased, and somewhere in the neighborhood of 10°C. the decline became rapid, with failure to respond altogether around 5°C. If cooling was discontinued at that temperature, the process was still reversible, since complete recovery occurred when the nerve was rewarmed.

Few clinical observations have been made on the effect of cooling on cutaneous sensation, although the numbing effects of cold, particularly that applied to the extremities, is a daily observation during ordinary winter exposure. Gammon and Starr,[3] in the course of studies on pain relief by counter-irritation, found that cold was most effective when applied to the skin at a temperature of 4 to 10°C. They observed cold to be more effective in relieving pain caused by irritant surface ointments than electricity, heat, vibration or air-jet stimulation. They accounted for the principal effect of cold in relieving pain on the basis of a decreased peripheral sensory discharge due to lowering of the temperature of the pain endings.

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### EXPERIMENTAL OBSERVATIONS

Experiments were undertaken to determine the feasibility of quick-cooling a small area of skin to a degree that would permit painless insertion of a needle. The area of skin that need be cooled for any one injection is small; it need remain cooled to an effective degree only long enough to carry out introduction of the needle — fifteen to thirty seconds. A small portable instrument capable of quickly cooling the skin to a degree sufficient to inhibit the cutaneous pain receptors temporarily but not producing pain in itself or any irreversible alterations in the skin or cutaneous receptors involved seemed desirable. Such an instrument, to be of practical value, demanded simplicity and suitability for use by nurses without danger of local skin damage.

After preliminary experiments with carbon dioxide snow in various types of containers, a much simpler instrument was constructed and has proved satisfactory for certain fundamental observations and for the carrying out of numerous clinical trials. A brass cylinder, 5 cm. in diameter and 22.5 cm. long, closed at one end, was selected. A smaller brass cylinder, 1 cm. in diameter and 1 cm. in length, was soldered on to the middle of the closed end of the larger cylinder. This small cylinder was filled with solder (20 per cent lead and 80 per cent tin), a rapid conductor of heat. The large cylinder was wrapped with felt 0.5 cm. in thickness. It was filled with cracked ice to which was added anhydrous calcium chloride. The open end of the cylinder was occluded by a tightly fitting rubber cork. The opposite, or contact end, was covered by a hollowed-out, closely fitting rubber cap. This gave a compact insulated instrument with a cooled round metallic contact surface 1 cm. in diameter (Fig. 1). It was found that with cracked ice alone in the brass cylinder, the temperature of the contact surface, as determined by an iron-constantan thermocouple (L. & N. Potentiometer), was about 7.5 to 9.5°C. By the addition of varying amounts of calcium

chloride to the cracked ice the temperature of the contact surface could be reduced as low as —4°C. If the cylinder was kept completely insulated — that is, with the rubber cap over the contact surface except when in use — the temperature of the contact remained at approximately the same level for several hours. If the instrument remained in a refrigerator when not in use, the temperature of the contact could be kept at desired levels for longer periods.

Numerous observations were first made on healthy subjects, to determine the effectiveness of this cooling metallic contact in reducing the skin temperature. These were made at room temperatures of 21 to 28°C. Skin temperatures were recorded from a potentiometer with the use of an iron-constantan thermocouple. Tests were made on many skin areas, notably those generally used for hypodermic injections: the lateral aspect of the upper arm, the lateral and dorsal aspects of the thigh, the lateral aspect of the buttock and the volar and dorsal surfaces of the forearm.

It was soon determined that when the skin temperature was reduced to a point between 11 and 14°C., preferably below 13°C. (normal skin temperature equals 31 to 34°C.), an ordinary No. 23 to 19 hypodermic needle could be introduced through the cooled skin without pain. This proved to be consistent in different subjects, at different testing periods and on different areas of skin. Pressure was perceived by the subject as the needle was pushed through the cooled skin, but no pain. If the cooled skin was elevated and pinched between the operator's thumb and index finger so as to exert counterpressure, there was no sensation when the needle was inserted.

Experiments were performed to determine the optimum temperature of the metal contact. It was found that a contact temperature of 4 to 6°C. proved most satisfactory. If the temperature was below 4°C., application of the contact became uncomfortable and, in areas of thin skin, such as the volar aspect of the forearm, definitely painful, owing to a local burning and aching sensation. If the temperature was above 7°C., the skin was not cooled to the critical level found essential for temporary inhibition of cutaneous pain receptors. The ideal temperature, therefore, was ±5°C. It was found that 25 gm. of anhydrous calcium chloride added to the 400 cc. of cracked ice in the instrument used consistently produced this temperature of the metal contact.

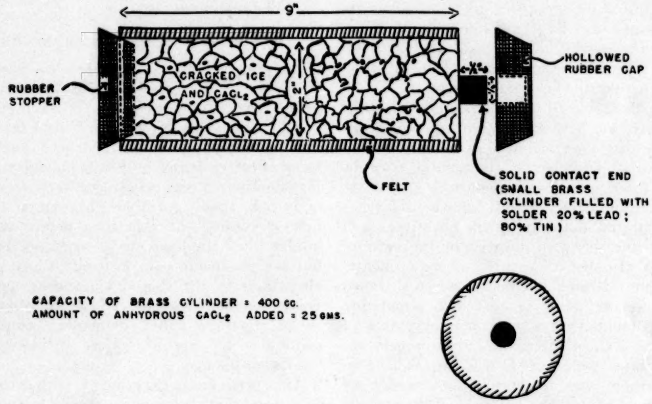
9"
RUBBER STOPPER
CRACKED ICE AND CaCl2
HOLLOWED RUBBER CAP
FELT
SOLID CONTACT END (SMALL BRASS CYLINDER FILLED WITH SOLDER 20% LEAD; 80% TIN)
CAPACITY OF BRASS CYLINDER = 400 CC.
AMOUNT OF ANHYDROUS CaCl2 ADDED = 25 GMS.

FIGURE 1. *Instrument for the Local Application of Cold.*

By determination of skin temperatures in various areas of the body after the contact had been applied at temperatures between 4.4 and 5.5°C. for varying periods, it was observed that forty-five to sixty seconds' cooling was adequate to reduce the skin temperature to the critical level for anesthesia (Fig. 2). The temperature remained within this range for thirty to sixty seconds. After that period, sensation gradually returned as the skin became warmer. The application of a tourniquet to the extremity proximal to the point of cooling did not affect the rate or degree of reduction of skin temperature by this method.

Cooling the surface of the skin did not lessen the discomfort of intradermal injections of fluid. After cooling of the skin to 11 to 13°C. an intradermal needle could be inserted entirely without pain, but subsequent injection of novocain or physiologic saline solution produced a momentary, intensely painful sensation, presumably by providing a different type of stimulus (distention of the skin), also be pain on actual injection into the substance of the muscle, depending on the nature and amount of the material injected.

It can also be used satisfactorily in routine venipunctures. The needle is inserted painlessly through a cooled area of skin immediately over or adjacent to a prominent superficial vein. Once through the skin there is little or no pain connected with seeking

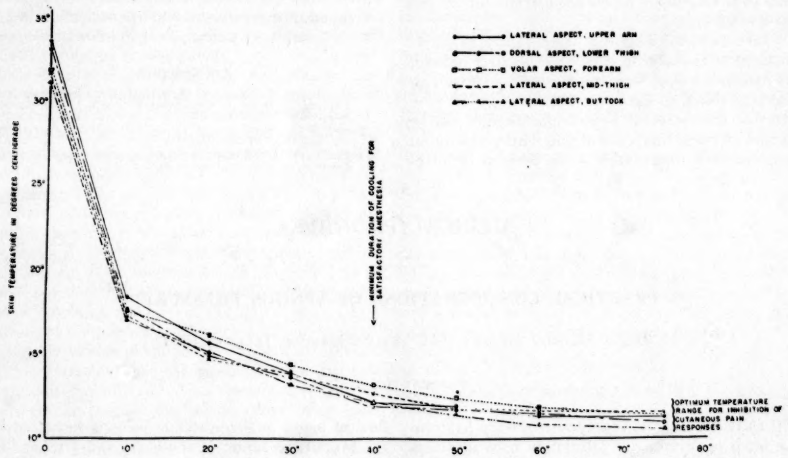


FIGURE 2. *Duration of Cooling with Metal Contact at 4.4 to 5.4°C. The time is expressed in seconds, and each point charted represents the average of three readings.*

which stimulated cutaneous endings not affected by the cooling. The method, therefore, is unsatisfactory for preliminary anesthesia of an area of skin subsequently to be anesthetized for prolonged insertion of a needle — as in lumbar puncture.

## CLINICAL APPLICATION

The application of this principle of local quick-cooling of the skin is widest naturally for subcutaneous injections; these can be done entirely without pain by the application of a metal contact whose temperature is ±5°C. to an area of skin for forty-five to sixty seconds, especially if the pressure of insertion of the needle is eliminated by counter-pressure on the adjacent skin. A metal contact at 5°C. feels cold but is not uncomfortable in that length of time except over areas of extremely thin skin. On the lateral aspect of the upper arm, the thigh and the buttock it is not at all unpleasant. The method is extremely effective for intramuscular injections, although occasionally slight twinges of pain are felt as the fascia is pierced, and there may the lumen of the vein with the point of the needle. If the procedure takes longer than sixty seconds owing to the operator's inability to insert the needle into the vein promptly, manipulations of the needle at the skin surface will again be painful.

This device has been used as follows on numerous children, as well as on adult patients. If old enough, the patient is told about the purpose of the cooling metal disk. Since most patients have had previous painful injections, they are receptive to its use. The skin area to be injected is prepared as usual by being wiped clean with an alcohol or Zephiran sponge. The rubber cap is removed from the cold contact surface, and the latter is also wiped with an alcohol or Zephiran sponge. The contact surface is held against the cleaned skin for forty-five to sixty seconds. The cooled skin is then gently elevated by squeezing together of the adjacent skin on either side, and injection performed through the center of the cooled area within thirty seconds. If patients looked away they were frequently entirely unable to tell the moment of insertion of the needle.

This method of local quick-cooling has been used satisfactorily for all types of subcutaneous medications, intramuscular chemotherapy, venipuncture for removal of blood and administration of drugs and for the insertion of subcutaneous clyses.


### Summary

When the skin temperature is reduced to 11 to 13°C. by external application of cold to a small area, pain responses to cutaneous stimuli in this area are inhibited.

A smooth metal disk at a temperature of ±5°C. held against the skin for forty-five to sixty seconds will reduce the skin temperature to 11 to 13°C. for periods of thirty to sixty seconds.

During that interval hypodermic needles can be inserted through the cooled skin entirely without pain, and with no sensation if the pressure of introduction of the needle is equalized by counter-pressure on the adjacent skin.

Reducing the skin temperature locally to this level is without danger, produces no irreversible changes and is not uncomfortable.

The method has been found useful, particularly in children, for the carrying out of painless hypodermic injections and all forms of parenteral therapy.

Any simple device, such as the one described above, that will provide a small metallic surface at a temperature consistently in the neighborhood of 5°C. is suitable for practical use in office or hospital.


### References


1. Denny-Brown, D., Adams, R. D., Brenner, C., and Doherty, M. M. Pathology of injury to nerve induced by cold. *J. Neuropath. & Exper. Neurol.* **4**:305-323, 1945.
2. Gasser, H. S. Nerve activity as modified by temperature changes. *Am. J. Physiol.* **97**:254-270, 1931.
3. Gammon, G. D., and Starr, I. Studies on relief of pain by counter-irritation. *J. Clin. Investigation* **20**:13-20, 1941.


## MEDICAL PROGRESS

## PRACTICAL CONSIDERATIONS OF VENOUS PRESSURE*


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CLINICAL interest in venous pressure has centered mainly on the alteration in its measurement in cases of heart disease.[1–7] In this connection most of the literature on the subject is concerned with the utility of venous-pressure measurement in confirming the diagnosis and following the progress of congestive heart failure. In addition, in the past few years the results of studies of venous pressure in its relation to the mechanism of heart failure have provoked a lively debate. At the same time there have been noteworthy improvements in technic of measurement, as well as increasing awareness of the value of the test in the diagnosis and study of a number of other conditions, including pericarditis, thoracoplasty, shock and a variety of causes of localized venous obstruction.

### Normal Physiology

Before the clinical application of venous-pressure measurement is reviewed, it seems advisable to recall briefly the normal physiology of venous flow. It is obvious at the start that the initial impetus to flow of blood in the systemic veins is imparted by the propulsive action of the heart and arteries. Of course, the capillary bed has a dampening effect on this action, so that the rate and volume of blood flow in the veins are more directly related to capillary pressure and flow. It is essential to remember also that the veins adjust their capacity nicely to the volume of blood delivered by the capillaries, this adjustment depending on the same nervous and humoral influences that affect arteriolar and capillary tone. At the other end of the venous circulation the heart has an important regulatory effect because of its ability normally to alter its output to suit wide variations in the volume of venous return. On this account, stagnation of blood in the veins is prevented under conditions in which venous return is increased. The flow of blood through the systemic veins receives another important propulsive force from the tone and intermittent contraction of the skeletal muscles. This force moves blood only in the direction of the heart because of the arrangement of the venous valves. Another factor that exerts a major influence in favor of venous return is the negative intrathoracic pressure. This produces an expansion of the thin-walled intrathoracic veins so that venous blood tends to be sucked into the thorax. Since the negative pressure in the thorax increases during inspiration and decreases during expiration, venous pressure fluctuates accordingly during the


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phases of respiration. Finally it must be mentioned that gravity influences venous flow and venous pressure. It is generally accepted that the right atrium represents the zero hydrostatic level for the blood in the veins — that is, the level at which gravity has no influence. In a vein located below this level, therefore, part of the venous pressure represents the weight of the column of blood interposed between the vein and the right atrium. It must be kept in mind that the effect of gravity is minimized by several mechanisms, including intramuscular pressure, muscle contraction, intra-abdominal tension and the system of venous valves.

Although there are numerous variables in the physiology of venous flow, some of them counterbalance in such a manner that venous pressure tends to be remarkably constant in normal subjects. In addition, the technic of measurement of venous pressure removes other variables. Before the measurement is made the patient is required to rest in bed for fifteen to thirty minutes. This prevents any alteration that might otherwise result from the effect of exertion.[2] During the test the patient is supine with the arm at an angle of 45° to the body and in such a position that the antecubital vein to be used is at or just below the level of the right atrium. This position of the arm eliminates any tendency to compression or torsion of the axillary or subclavian vein, which may result when the arm is closer to the side or more fully abducted.[2] Also, the fact that the vein selected for venipuncture is not above heart level prevents errors in measurement that might otherwise result from collapse of such superficial veins.[2] An effort is made to have the patient relax fully, so that muscle tension will not alter the results, and he is instructed to breathe easily and regularly to avoid the effects of alteration of the intrathoracic pressure. Apnea, sighing, straining, coughing, talking and other variations in the respiratory act prevent accurate evaluation of the venous pressure.[4] The supine position minimizes the effect of gravity, and in addition, the hydrostatic factor should be entirely eliminated by the use of a level for reference of the venous-pressure measurement at which hydrostatic pressure is zero.

A number of different zero levels have been used, and this has naturally led to some variation in the values reported for normal venous pressure.[2, 3] Needless confusion has developed concerning the significance of this point. As a matter of fact, the selection of the zero level has made little practical difference in the results reported by various authors, except that the results must be evaluated individually and cannot be used interchangeably. The situation is analogous to that which obtains in connection with a laboratory test like the erythrocyte sedimentation rate. Various technics have been used, and the values found with one technic are not the same as those with another, although they are individually valid. There is much to recommend the zero level selected by Lyons, Kennedy and Burwell[2] at a point 10 cm. from the skin of the patient's back when the supine position is utilized. This level closely approximates the plane of the right atrium and agrees remarkably well with results obtained by Holt[8] in a detailed study of the problem of eliminating the hydrostatic factor during venous-pressure measurement. Winsor and Burch[9] advocate the use of the "phlebostatic axis" to find the zero level for reference. They define the axis as a line resulting from the intersection of a frontal plane passing midway between the posterior surface of the body and the base of the xiphoid process, with a cross-sectional plane passing through the fourth intercostal space adjacent to the sternum. A horizontal plane passing through this axis is the phlebostatic level. The use of this level is recommended by its originators because it is supposed to give the same results regardless of the position of the patient. This appears to be true for normal persons but is far from true for patients with venous hypertension from any cause,[3, 4] so that the arguments in favor of employing this reference level lose their force. With the patient supine the same reference level that is used for measurement of the venous pressure in the arm veins should be used for those in other veins, such as the femoral, for purposes of comparison.

## Technics

The numerous variations in technic for measurement of venous blood pressure can be grouped in three categories, as follows: clinical inspection of superficial veins, the indirect method and the direct method.

### *Clinical Inspection of Superficial Veins*

Inspection of suitable superficial veins is useful for estimation of the venous pressure only when the pressure is higher than normal, so that the veins are abnormally distended. Probably the most widely employed technic entails inspection of the external jugular veins.[10, 11] When a patient is in a semi-sitting position, these veins normally are not filled above the plane of the manubrium. Distention of the veins above this level indicates that the venous pressure is abnormally high, at least in the superior-vena-cava system (Fig. 1). This finding in a patient who also has hepatomegaly with or without edema of the lower part of the body permits the conclusion that there is a generalized elevation of the venous pressure above normal, such as that in congestive heart failure. At times in heart failure, abnormal distention of the jugular veins is not detected until the abdomen is firmly compressed, or this maneuver may increase the amount of distention (hepatojugular reflux). This point is discussed below in full.

Another technic for determining that the venous pressure is abnormally high was originally described by Gaertner.[13, 14] With the patient sitting and relaxed, the superficial veins of the hand are watched

for collapse while the arm is slowly raised. The distance of the point at which collapse is observed from the plane of the right atrium (taken as the fourth intercostal space) is a rough measurement of the venous pressure. Normally, it is equivalent to 100 mm. of water.

In a third technic the veins on the undersurface of the tongue are inspected while the patient is sitting.[15] When the venous pressure is equivalent to more than about 200 mm. of water these veins are obviously distended; normally, they are collapsed.

The inspection procedures described above afford a rough qualitative means for evaluation of the venous pressure, mainly in cases of heart failure. When the findings are positive it is fairly safe to conclude that the venous pressure is higher than normal, although rather wide variations of degree cannot be assayed. When the findings are negative it is not safe to conclude that the venous pressure is within normal limits. This is true because a patient with heart failure, for example, may have a high venous pressure while supine and normal venous pressure while sitting.[3, 4] Elevated pressure of long duration is more likely to show clinically detectable venous distention than when it is of recent onset. Superficial veins in elderly persons are occasionally sclerotic and do not readily distend or collapse with variations in venous pressure.

Inspection of the superficial veins is a much more reliable diagnostic aid for detection of localized venous obstruction. The pattern of the superficial veins in the distribution of the collateral circulation of the obstructed vein contrasts so distinctly with the appearance of the superficial veins elsewhere that suspicion of the diagnosis is obtained with the first glance. Two words of caution may be valuable regarding this point. In the first place, there are considerable differences in the visibility of the superficial veins of different persons, depending on the quality of the skin as well as anatomic variations in the venous pattern. It is important to remember, therefore, that the superficial veins must be distended, not merely visible, before they are accepted as evidence of localized venous obstruction. Secondly, there is probably a great tendency to overlook the fact that distention of the superficial veins more frequently indicates local obstruction of the deep veins than vice versa. An excellent example of this tendency is in cases of varicose veins of the lower extremities, which the physician often treats as a cosmetic problem without troubling to decide whether or not they are a consequence of deep venous occlusion.

*Indirect Method*

The indirect method of measurement of venous pressure no longer has wide popularity, although it was extensively employed by Eyster[1] and a few other workers.[16] It depends on the principle that the least pressure necessary to cause collapse of a vein is approximately equal to the pressure within its lumen. The main advantage of this method is that since venipuncture is avoided it can be used frequently and painlessly in the same patient. This advantage is outweighed by many disadvantages, including the difficulty of learning to use the apparatus skillfully, the failure of the test when the superficial veins are sclerotic or not visible and the fact that the venous wall may manifest hypertonus in some cases of heart failure.

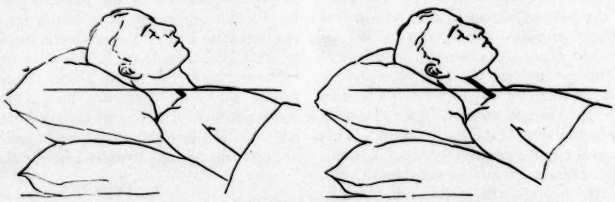

FIGURE 1. *Normal and Distended External Jugular Vein.*
*The sketch on the left demonstrates an external jugular vein normally filled; that on the right shows an external jugular vein filled to an abnormal height as a result of increased venous pressure (reproduced from Hussey[12] by permission of the publisher).*

*Direct Method*

The direct method is the one most generally employed when results more accurate than those that can be obtained by simple inspection of the veins are desired. It consists essentially of measuring the venous pressure through a needle that has been inserted into the vein. A variety of instruments have been devised for this purpose.[12, 17–27] Most of them adopt the principle of a liquid manometer so that the measurement is represented directly as millimeters of physiologic saline solution, the liquid usually employed. An apparatus of this type that has given satisfaction during extensive trial is shown in Figure 2. This instrument is sterilized by boiling or autoclaving before it is used. It consists of a glass measuring tube (*A*) having a 3-mm. or 4-mm. bore and attached by rubber tubing to a three-way stopcock (*C*). Affixed to the appropriate adapters of the stopcock are a 5-cc. or 10-cc. syringe (*B*) con-

taining sterile saline solution and a 19-gauge or 20-gauge needle 3.7 cm. long (*D*). The rubber tubing and glass rod are filled from the syringe, and the stopcock is then turned so that solution from the syringe can be injected into the vein to be punctured. It the venous pressure only is to be measured, the syringe is left partly filled with saline solution. If the circulation time is to be measured as part of the procedure, the syringe is filled with the agent used for this purpose. After venipuncture, the stopcock is turned to the position that permits the solution to enter the vein from the measuring tube. Details regarding the position of the patient and

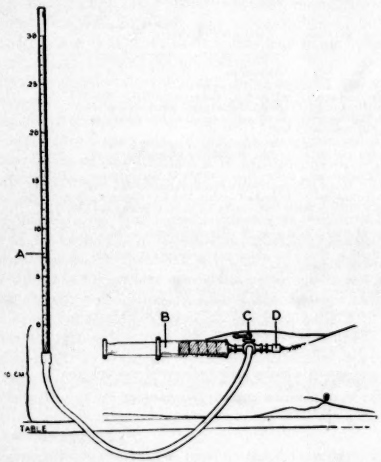


FIGURE 2. *Apparatus for Measurements of Venous Pressure (Reproduced from Hussey[12] by Permission of the Publisher).*

other essentials of technic during the procedure have been discussed above. For the moment, it is sufficient to say that the column of liquid in the measuring tube fluctuates lazily with respiration and sometimes sharply with the arterial pulse. The introduction of a needle into the vein may produce a temporary venospasm, which tends to raise the venous pressure. Ordinarily, the effect disappears within so short a time as to be a negligible factor. The tendency of the initial high value to drop to a constant level has been called "venous pressure drift."[3]

The apparatus described, although entirely suitable in hospital practice, is not completely satisfactory for routine use as a part of the examination equipment of the average physician. With this consideration in mind Burch and Winsor[21] have devised the "phlebomanometer." This instrument adapts the principles of the aneroid manometer used clinically for recording arterial blood pressure to a manometer sensitive enough to register venous pressure. It is compact and portable and appears simple enough to be popular.

The instruments for direct measurement of venous pressure can be used in any accessible vein. The discussion presented below indicates that in some cases it is desirable to compare measurements in several different veins in the same patient. In the lower extremity the best vein for such comparisons is the femoral.[24, 25] This vein is punctured according to the technic of Griffith, Chamberlain and Kitchell[18] by insertion of a needle upward and inward at a point 2.5 cm. distal to the inguinal ligament and just medial to the pulsation of the femoral artery. No tourniquet is required. The angle that the needle makes with the skin of the thigh and the depth to which it is introduced must be varied with the thickness of the tissues overlying the femoral vessels. For almost all cases a needle 3.7 cm. long is adequate.

Other veins in the lower extremity than the femoral may be utilized for venous-pressure determinations. A number of French clinicians favor the use of the greater saphenous near the femoral triangle in place of the femoral vein.[28–30] If the greater saphenous vein at a lower level or the dorsal pedal vein is used, due consideration must be given to the gradient of pressures the more distal the vein is located from the heart.[3, 31] For example, in a typical case the pressure of the dorsal pedal vein was 40 mm. more than that in the greater saphenous vein at a higher level.[3] The problem of gradient of pressures has been well discussed by Winsor and Burch[3] and Burton–Opitz.[31] This pressure gradient also holds for the upper extremity. For example, the dorsal-metacarpal-vein pressure may be about 10 mm. higher than that in the median basilic and 50 mm. higher than that in the cephalic or jugular vein.[3] Measurements of the pressure in the popliteal veins have also been made in a study of the effects of localized obstruction to venous flow in the lower extremities.[32] For this purpose the patient is standing and the "local" venous pressure only is measured by means of a mercury manometer. The difficulties of technic will prevent this method from being used except for research. Venous pressure may also be determined in the internal or external jugular vein.[33, 34]

## NORMAL VALUES

Normal values for venous pressure measured by the direct method have varied in the experience of different authors on account of technical differences in their studies. The principal reason, as mentioned above, has been the lack of uniformity for selection of the zero level for reference of the measurement. When the zero level is placed at a point 10 cm. from the skin of the patient's back, the venous pressure

in the arms is normally equivalent to 50 to 150 mm. of saline solution.[2] The values reported by Winsor and Burch[3] using a slightly different zero level were essentially the same. Normally, the pressure in the femoral vein is usually about equal to or a little higher than that in the antecubital vein of the same person.[5, 24, 25] In some subjects, particularly those who are obese, the femoral-vein pressure may be as much as 40 mm. of saline solution higher than the antecubital pressure.

According to Jacques[26] there appears to be little difference between venous pressures in adults and children when they are considered collectively and studied under the same conditions of technic. Eighty-three per cent of measurements were equivalent to between 80 and 130 mm. of water. Lambert[27] has also reported on venous-pressure values in normal children.

Table 1. *Diagnostic Value of Regional Differences in Venous Pressures.*

| Pressure Data | Diagnosis |
|---|---|
| Diminished in all peripheral veins | Peripheral vascular collapse (shock); syncope. |
| Elevated in all peripheral veins | Right-sided and generalized cardiac failure; constrictive pericarditis (Pick disease); pericardial effusion; uniform loss of negative chest pressure (obstructive emphysema); Bernheim syndrome; varicose veins. |
| Normal arm and elevated in leg veins* | Ascites; tympanites; pneumoperitoneum; pregnancy; hypernephroma and other tumors of kidney, with invasion of inferior vena cava; primary carcinoma of liver, with invasion of inferior vena cava; primary tumor of inferior vena cava; thrombosis of inferior vena cava; ligation of inferior vena cava; masses in peritoneal cavity; solitary abscess in right lobe of liver; subphrenic abscess on right; echinococcus cyst of liver; large tumor mass in right lobe of liver. |
| Elevated in arm and normal in leg veins | Aneurysm of aorta; ?dilatation of aorta; lymphoma of mediastinum; metastatic masses in mediastinum; primary tumor of mediastinal structures; abscess of mediastinum; thrombosis of superior vena cava. |
| More elevated in one arm than in other and lower or normal in leg veins | Localized obstruction of axillary or subclavian veins due to exertion, pressure from neoplasm, cardiac failure; unilateral chest lesions (pleural effusion, pneumothorax, thoracoplasty); aneurysm of aorta (85% higher on left than on right); aneurysm of innominate artery (higher on right than on left); arteriovenous fistula of arm. |
| More elevated in one leg than in other and lower or normal in arm veins | Arteriovenous fistula of leg; thrombosis of femoral or iliac vein. |
| Dissociation between internal jugular vein and general peripheral venous system | Polycythemia or mass in neck or upper mediastinum (elevated pressure); thrombosis of lateral sinus (diminished pressure). |
| Elevated in portal vein and normal in arm and leg veins | Cirrhosis of liver; obstruction of portal vein; obstruction of splenic vein; ?Chiari syndrome. |

*Also observed during abdominal operations.

## Response to Exercise

Venous-pressure response to exercise, under certain conditions, affords a means of enhancing the value of the determinations. A reasonably extensive literature exists on this subject. This has been reviewed by Szekely.[35] A standardized technic for measuring venous pressure during and after exercise has been devised and gives reasonably consistent results.[35] In normal subjects the venous pressure rises from 20 to 50 mm. of water during exercise and returns to or slightly below the basal level within thirty seconds after cessation of the exercise.[35] In patients with heart failure it rises much higher with exercise and returns to the initial level more slowly.[35] This may be true even though the resting venous pressure of such a cardiac patient is normal. In a group of patients with cardiac disease and without evidence of heart failure Szekely[35] noted that some showed a pathologic response. Presumably, these were cases of latent cardiac failure. These studies in human beings are interesting in view of the demonstration by Landis[36] that experimental damage to the heart of the dog did not produce a rise in venous pressure until the effect of exercise was superimposed. On the basis of his experiments Landis commented that this could explain the development of right-upper-quadrant pain and a palpable liver after exercise in a cardiac patient whose resting venous pressure is normal.

When venous outflow from an extremity is obstructed locally, exercise of the extremity causes a progressive increase in venous pressure above the resting level, and return to this level is slow.[32, 37] This technic can be readily employed when the upper extremity is involved.[32, 37]

The exercise of the upper extremity consists of repeated clenching of the fist for one minute. Normally, the venous pressure falls slightly or remains stationary except for minor fluctuations during the exercise. Local obstruction anywhere from the axillary vein to the superior vena cava produces a steady increase in venous pressure during the one minute of the exercise test. The magnitude of the rise varies from 10 to 900 mm. of water.[32, 37] This hand-clenching exercise is without effect in cardiac patients presumably because it is not strenuous enough to cause a general effect. Similar results are obtained when the popliteal vein is used to test for obstruction of veins of the lower extremity or pelvis.[32, 37] In constrictive pericarditis, the effect of local exercise (clenching fists) may be the same as in cases of local venous obstruction of the upper extremity in con-

trast to what is obtained in cardiac failure.[32, 38] This has been noted in 3 typical cases.[32, 38]

### Hepatojugular Reflux

It was mentioned above that distention of the cervical veins in heart failure may become apparent for the first time when the patient's abdomen is firmly compressed. This phenomenon was originally described by Pasteur[39] and later by Rondot.[40] It has since been called the hepatojugular reflux and also the Pasteur-Rondot phenomenon. The use of this maneuver has been commented on by Fishberg[41] and extensively studied by Oppenheimer and Hitzig[7] and by Hitzig.[32, 42] It depends on the fact that abdominal compression quickly increases the return of blood through the inferior vena cava from the congested viscera, especially the liver, so that, in a sense, there is competition of this augmented flow with blood arriving from the superior vena cava. Because the heart is failing, the increased venous return is not accommodated, and consequent stagnation of blood in the superior vena cava is reflected as an increase in venous pressure in the tributaries of this vessel.[7] The same effect may be expected when there is a general increase in venous pressure from some other cause, such as constrictive pericarditis or pericardial effusion. When the superior vena cava is extensively obstructed the same phenomenon is observed, although the mechanism is different.[32, 43] Here the effect of compression of the abdomen is to impede flow of blood through the inferior vena cava. Since in this syndrome this is the main route for ingress of blood from the superior-vena-cava system as well, pressure rises in the veins of this system. A similar result is obtained when the large superficial collateral veins of the trunk are occluded by means of a band encircling the thorax.[32]

For obvious technical reasons the influence of abdominal compression on venous pressure can best be evaluated by direct measurement. When an initial reading of the venous-pressure measurement has been obtained by the technic described above, the examiner compresses the patient's abdomen, preferably the right upper quadrant, for one minute. Care is taken to apply the compression gradually so that there will be no interference with the rate, rhythm or depth of respiration and no tendency for the patient to tense his muscles. Normally, with the maneuver, the pressure in the antecubital vein remains unchanged or falls.[3, 4, 42] This effect is explained by the fact that curtailment of venous return from the inferior vena cava encourages a more rapid emptying of the superior-vena-cava system. In conditions causing general elevation of the venous pressure above normal and in the superior-vena-cava syndrome, the maneuver causes a rise of 10 mm. or more of water in the arm-vein pressure. It is of considerable diagnostic importance that in cases of mild or latent heart failure the same effect is obtained, although the venous pressure initially may be within normal limits.[3, 4, 42] It has also been demonstrated that the venous pressure in the arms rises 30 mm. or more in patients with heart failure when the legs are raised from the bed while the trunk remains horizontal (Azoulay position).[42, 44] This finding has a significance equivalent to the hepatojugular reflux.

### Relation of Spinal-Fluid to Systemic Venous Pressure

It is well established scientifically that a close relation exists between spinal-fluid pressure and cerebral venous pressure.[45] Except under certain rare conditions in which there is a dissociation between the internal jugular-vein and arm-vein pressures, which is discussed in greater detail below, the cerebral venous pressure reflects the general systemic venous pressure[45–47] or occasionally the pressure existing in the superior-vena-cava system.[33] A number of practical points about this relation are frequently overlooked in clinical practice.

The spinal-fluid pressure is increased in any of the conditions listed under the heading "elevated venous pressure in all peripheral veins" in Table 1 and in any other disease referred to in the table that involves the venous return through the superior vena cava. Harrison[45] found in normal people, as well as in patients with cardiac failure and elevated venous pressure, a definite ratio of spinal-fluid pressure to venous pressure that averaged 1.6. Therefore, if a spinal-fluid pressure is found to be elevated and no central-nervous-system disease appears to be the cause, a check on the arm-vein pressure is indicated. Increased spinal-fluid pressure secondary to high venous pressure has been suggested as the cause of a number of central-nervous-system manifestations.

*(To be concluded)*

### References


1. Eyster, J. A. E. *The Clinical Aspects of Venous Pressure.* 135 pp. New York: Macmillan Co., 1929.
2. Lyons, R. H., Kennedy, J. A., and Burwell, C. S. Measurement of venous pressure by direct method. *Am. Heart J.* **16**:675-683, 1938.
3. Winsor, T., and Burch, G. E. Use of phlebomanometer: normal venous pressure values and study of certain aspects of venous hypertension in man. *Am. Heart J.* **31**:387-406, 1946.
4. Hussey, H. H., Wallace, J. J., and Sullivan, J. C. Value of combined measurements of venous pressure and arm-to-tongue and arm-to-lung circulation times in study of heart failure. *Am. Heart J.* **23**:22-36, 1942.
5. Griffith, G. C., Chamberlain, C. T., and Kitchell, J. R. Observations on practical significance of venous pressure in health and disease with review of literature. *Am. J. M. Sc.* **187**:642-649, 1934.
6. Fishberg, A. M. *Heart Failure.* Second edition. 829 pp. Philadelphia: Lea & Febiger, 1940. Pp. 96-114.
7. Oppenheimer, B. S., and Hitzig, W. M. Use of circulatory measurements in evaluating pulmonary and cardiac factors in chronic lung disorders. *Am. Heart J.* **12**:257-271, 1936.
8. Holt, J. P. Measurement of venous pressure in man eliminating hydrostatic factor. *Am. J. Physiol.* **130**:635-641, 1940.
9. Winsor, T., and Burch, G. E. Phlebostatic axis and phlebostatic level, reference levels for venous pressure measurements in man. *Proc. Soc. Exper. Biol. & Med.* **58**:165-169, 1945.
10. Lewis, T. Remarks on early signs of cardiac failure of congestive type. *Brit. M. J.* **1**:849-852, 1930.
11. Fishberg.[6] P. 112.
12. Hussey, H. H. Venous blood pressure and circulation times. In *The Practitioner's Library of Medicine and Surgery (1940 Supplement).* Edited by G. Blumer. 771 pp. New York: D. Appleton-Century Co., 1941.

13. Gaertner, G. Die Messung des Drucks im rechten Vorhof. *München. med. Wchnschr.* 51:212, 1904.
14. Robertson, H. F. Clinical method of venous pressure determination. *J. A. M. A.* 101:206, 1933.
15. May, A. M. Tongue sign for high venous pressure. *Am. Heart J.* 26:685, 1943.
16. Krogh, A., Turner, A. H., and Landis, E. M. Celluloid capsule for measuring venous pressures. *J. Clin. Investigation* 11:357-362, 1932.
17. Moritz, F., and von Tabora, D. Über ein Methode, beim Menschen den Druck in oberflächlichen Venen exakt zu Bestimmen. *Deutsches Arch. f. klin. Med.* 98:475-505, 1910.
18. Griffith, G. C., Chamberlain, C. T., and Kitchell, J. R. Simplified apparatus for direct venous pressure determination modified from Moritz and v. Tabora. *Am. J. M. Sc.* 187:371-376, 1934.
19. Taylor, F. A., Thomas, A. B., and Schleiter, H. G. Direct method for estimation of venous blood pressure. *Proc. Soc. Exper. Biol. & Med.* 27:867-871, 1930.
20. Cohen, L. New instrument for determination of venous pressure by direct method. *J. Lab. & Clin. Med.* 22:94-96, 1936.
21. Burch, G. E., and Winsor, T. Phlebomanometer: new apparatus for direct measurement of venous pressure in large and small veins. *J. A. M. A.* 123:91, 1943.
22. Veal, J. R., and Hussey, H. H. Changes in pressure in antecubital and saphenous veins during abdominal operations. *Surgery* 7: 809-818, 1940.
23. Villaret, M. Quoted by Fishberg.[6] P. 113.
24. Hussey, H. H. Effect of mediastinal lesions on pressures in antecubital and femoral veins: report of 52 cases. *Am. Heart J.* 17: 57-68, 1939.
25. Ferris, E. B., Jr., and Wilkins, R. W. Clinical value of comparative measurements of pressure in femoral and cubital veins. *Am. Heart J.* 13:431-439, 1937.
26. Jacques, L. H. Venous pressure in children. *J. Iowa State M. Soc.* 32:294-296, 1942.
27. Lambert, J. P. Venous pressure in children. *Am. J. Dis. Child.* 52:1088-1092, 1936.
28. Villaret, M., and Martiny, M. Étude de la pression veineuse périphérique dans les syndromes médiastinaux: son intérêt de contrôl pour le diagnostic et le pronostic. *Presse méd.* 37:249-251, 1929.
29. Villaret, M., Saint Girons, F., and Bosviel, G. La pression veineuse périphérique au cours des syndromes d'hypertension veineuse localisée. *Bull. méd.* 39:821-831, 1925.
30. Villaret, M., and Desoille, H. Quelques exemples cliniques montrant l'intérêt général de la phlébopiézométrie au point de vue du diagnostic, du pronostic et de la thérapeutique. *Presse méd.* 40:1477-1480, 1932.
31. Burton-Opitz, R. Venous pressures. *Am. J. Physiol.* 9:198-213, 1903.
32. Veal, J. R., and Hussey, H. H. Use of "exercise tests" in connection with venous pressure measurements for detection of venous obstruction in upper and lower extremities: preliminary report *Am. Heart J.* 20:308-321, 1940.
33. Hitzig, W. M. On mechanisms of inspiratory filling of cervical veins and pulsus paradoxus in venous hypertension. *J. Mt. Sinai Hosp.* 8:625-644, 1942.
34. Loman, J., and Dameshek, W. Increased intracranial venous and cerebrospinal fluid pressures in polycythemia. *Tr. Am. Neurol. A.* 70:84-87, 1944.
35. Szekely, P. Venous pressure responses to exercise: preliminary report. *Am. Heart J.* 22:360-366, 1941.
36. Landis, E. M., Brown, E., Fauteux, M., and Wise, C. Central venous pressure in relation to cardiac "competence," blood volume and exercise. *J. Clin. Investigation* 25:237-255, 1946.
37. Veal, J. R., and Hussey, H. H. Methods for measurement of pressures in antecubital and popliteal veins during exercise. *M. Ann. District of Columbia* 9:71-74, 1940.
38. *Idem.* Unpublished data.
39. Pasteur, W. Note on new physical sign of tricuspid regurgitation. *Lancet* 2:524, 1885.
40. Rondot, E. Le reflux hépato-jugulaire. *Gaz. hebd. d. sc. méd. de Bordeaux* 19:567-571, 579 and 590, 1898.
41. Fishberg.[6] P. 256.
42. Hitzig, W. M. Venous pressure curves in normal and abnormal circulatory states. I. Normal venous pressure curves and negative "hepato-jugular reflux phenomenon." *J. Mt. Sinai Hosp.* 12: 309-334, 1945.
43. Hussey, H. H., Katz, S., and Yater, W. M. Superior vena caval syndrome: report of thirty-five cases. *Am. Heart J.* 31:1-26, 1946.
44. Levin, E. La hipertensión venosa provocada como signo de insuficiencia cardíaca. *Semana méd.* 2:915-920, 1934.
45. Harrison, W. G., Jr. Cerebrospinal fluid pressure and venous pressure in cardiac failure and effect of spinal drainage in treatment of cardiac decompensation. *Arch. Int. Med.* 53:782-791, 1934.
46. Friedfeld, L., and Fishberg, A. M. Relation of cerebrospinal and venous pressures in heart failure. *J. Clin. Investigation* 13:495-501, 1934.
47. Myerson, A., and Loman, J. Internal jugular venous pressure in man; its relationship to cerebrospinal fluid and carotid arterial pressures. *Arch. Neurol. & Psychiat.* 27:836-846, 1932.

## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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### CASE 33471

#### PRESENTATION OF CASE

A sixty-four-year-old man entered the hospital because of pain in the left flank.

Eighteen years before admission the patient was told that he had bilateral kidney stones. Since that time frequent x-ray studies had been made, and the stones did not appear larger. He felt reasonably well until a year before entry, when he began to have malaise, anorexia, pallor and twinges of pain in the left flank. This pain became more frequent and severe, and for the previous month had been constant. It radiated from the flank to the lower back and groin and down the anterolateral aspect of the left thigh. There was nocturia (two or three times) and questionable hematuria.

The past history was irrelevant except for meningitis at the age of sixteen years, which had left the patient partially deaf in the right ear.

Physical examination revealed a thin, sallow man with a large, firm, tender, fixed mass in the region of the left kidney and a soft, apical systolic murmur. Neurologic examination disclosed bilateral Babinski reflexes, bilateral clonus, hyperactive reflexes, absent vibration sense at the right ankle, facial palsy on the right and Hoffmann's sign on the right.

The temperature was 100°F., the pulse 100, and the respirations 20. The blood pressure was 125 systolic, 70 diastolic.

Examination of the blood revealed a white-cell count of 15,600 and a hemoglobin of 7.5 gm. The urine gave a + test for albumin; the sediment contained only an occasional red and white cell per high-power field. The nonprotein nitrogen was 41 mg. and the total protein 6.4 gm. per 100 cc., and the alkaline phosphatase 5.7 Bodansky units. The carbon dioxide, chloride, calcium and phosphorus were within normal limits.

A plain x-ray film showed bilateral, irregular, stag-horn calculi (Fig. 1). On the left side there was also irregular calcification overlying the lower pole of the kidney. There were several smaller areas of calcification in the right paravertebral region and pelvis, one of which was in line with the ureter.

A cystoscopy with ureteral catheterization and retrograde pyelography was done. The bladder

showed numerous calculi lying over the floor and a rather marked trabeculation. At the vesical orifice there was some enlargement of the median portion of the prostate. The left ureteral orifice was catheterized without great difficulty, but after the catheter had ascended to the upper ureter, it could not be pushed through into the renal pelvis and no drainage of urine occurred and none could be

FIGURE 1. *Plain Film of the Abdomen.*

aspirated. On the right side a catheter passed easily to the kidney, and the passage of the catheter was followed by rather clear urine.

Retrograde pyelography on the right side showed opaque material in the lower group of dilated calyxes surrounding the calcification here as well as that in the kidney pelvis (Fig. 2). None of the material was seen to enter the upper group except possibly in one infundibulum. The group of calcifications in the midabdomen was outside the ureter. A small bit of calcification in the right pelvis was probably within the distal ureter, which was slightly widened. On the left side the opaque medium also projected into the lower group of calyxes and extended into the calcification in the lower pole. Medial to the left renal pelvis the dye was seen as mottled, irregular areas of increased density. None was seen in the ureter.

Cultures of urine from the bladder and right kidney were negative.

The patient was given a total of 2500 cc. of whole blood, which finally raised the hemoglobin to 11.4 gm. An operation was done on the tenth hospital day.

## DIFFERENTIAL DIAGNOSIS

DR. F. A. SIMEONE: This is the story of a sixty-four-year-old man who had calculi in both kidneys for ten years, but who had no symptoms from them, from an associated lesion or from an entirely new lesion until one year before entry. During this year he began to have malaise, anorexia, pallor and twinges of pain in the left flank. Taking for granted that he had stag-horn calculi and a few smaller calculi in the renal pelvis, these attacks might represent the repeated passage of small stones, perhaps culminating in increasing infection and possibly total obstruction of the kidney. The pain radiated from the flank to the lower back and

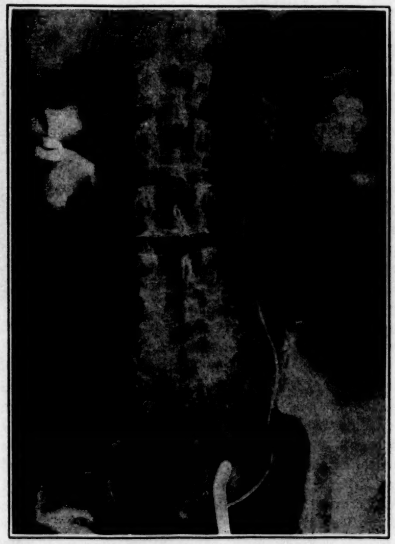

FIGURE 2. *Retrograde Pyelogram of Left Kidney.*

groin and to the anterolateral aspect of the left thigh. In the presence of a fixed palpable tumor in the left flank, this distribution of pain does not help further in the diagnosis but suggests that the mass was impinging on the lumbosacral plexus, thereby explaining the radiation of the pain into the thigh.

The past history was irrelevant.

In the physical examination the important point was the large, firm, tender, fixed mass in the left kidney region. I do not believe that the soft apical systolic murmur was of significance, particularly in the presence of anemia. Many neurologic signs were described, but I am unable to connect them with the lesion in the flank. If it was a tumor, I do not believe that we can assume that there were metastases to the brain on the basis of the findings given. What seems more probable is that the signs represented pyramidal-tract disease as a result of the arteriosclerosis.

The slightly elevated temperature and pulse rate are consistent with an inflammatory lesion in the region of the left kidney, although a malignant lesion is not ruled out, because even in the absence of demonstrated necrosis in the tumor, renal tumors or other large tumors in that region might be accompanied by febrile reactions. Examination of the blood showed a leukocytosis, which is again consistent with an inflammatory lesion, but does not rule out the possibility of a malignant lesion. The hemoglobin of 7.5 gm. per 100 cc., or approximately 50 per cent of what it should be, might be attributed to the urinary-tract infection for a matter of years, which we know this man had, and perhaps to the occasional bleeding into the urine as suggested by the questionable hematuria. There was a slight amount of albumin and only an occasional red and white cell per high-power field. The interesting point about that finding is that the urine did not disclose more abnormalities. The nonprotein nitrogen of 41 mg. per 100 cc. suggests some decrease in the function of the kidneys. The alkaline phosphatase was perhaps within the upper limits of normal. I do not believe that it suggests bone metastases. The calcium and phosphorus concentrations in the serum were within normal limits, which should rule out hyperparathyroidism.

We finally come to the x-ray examination, which yields more definite information. In the first place there were stag-horn calculi bilaterally, and on the left side irregular calcification overlying the lower pole of the kidney. There were several smaller areas of calcification in the right paravertebral region, one of which was in line with the ureter. As described, this makes one wonder whether the lesion was tuberculosis. There is nothing to suggest psoas abscesses with calcification in them. No mention is made of bone disease on x-ray examination, which one would expect under such circumstances. Since an intravenous pyelogram is not recorded I shall assume that it was not done, perhaps because the renal function was not considered adequate to yield a satisfactory pyelogram.

A cystoscopy was done and it gave some specific information. Numerous calculi were found in the floor of the bladder; these perhaps came down from the calculi in the kidney and may have come from the left kidney, thereby accounting for the twinges of left-flank pain that the patient had had during the preceding year. The enlargement of the median portion of the prostate is not particularly remarkable except that it helps to explain why these calculi were not passed from within the bladder.

We have the statement that the left ureteral orifice was catheterized without difficulty, but after the catheter had ascended to the upper ureter it could not be pushed through into the renal pelvis. No drainage of urine occurred, and none could be aspirated. That suggests an obstruction, perhaps in the upper ureter or at the ureteropelvic junction. Furthermore, however, on injection of a contrast medium some of the material did get into the pelvis, into the lower calyxes and actually into the region that contained the calcification. It is rather difficult to understand this obstruction to the passage of a catheter into the kidney when no great obstruction was demonstrable to the retrograde injection of dye, and particularly since there was no mention that dye was seen in the left ureter. With a degree of obstruction great enough to prevent the passage of a catheter but not of injected fluid, one would expect some of the solution to reflux down the ureter.

Perhaps we should see the x-ray films now.

DR. STANLEY M. WYMAN: The first few films are without dye. An additional point to be mentioned is the possibility of calcification in the left kidney. The calcification lies far lateral in relation to the lumbar spine. There is a suggestion of a mass overlying this portion of the abdomen contiguous with the kidney and perhaps displacing the calcification laterally. This is the calcification described overlying the lower pole. The next film shows the catheter right in the kidney pelvis. Again, the direction taken by the catheter suggests that the kidney is displaced. On the third film we see dye entering the right kidney and lying around the stone and outlining a normal ureter. The last film shows dye in the left kidney around the numerous small areas of calcification in the lower pole and also surrounding, to a slight extent, the large stag-horn calculus. The interesting part is this irregular distribution of dye. It represents perhaps the kidney pelvis and the area just above and medial to it. It is a lacy, irregular pattern of dye that suggests an irregular cavity of some sort, communicating with the kidney pelvis.

DR. SIMEONE: Do you think that this dye could be extravasated outside the urinary passage?

DR. WYMAN: I cannot say that it is not extravasated and lying free in the peritoneal cavity, but it seems unlikely. I should like to explain the displacement of the stone on some basis connected with this irregular accumulation of dye.

DR. SIMEONE: We now come to a differential diagnosis. This man had a tender fixed mass in the left flank. One wonders about lesions in the organs immediately adjacent to the kidney, such

as the descending colon, the spleen and the pancreas, but I think that we can pass these up because we have no data suggesting that these organs have been involved. We might concentrate on a differential diagnosis of the possible lesion that could cause this picture arising from the kidney itself. Before I saw the x-ray films I thought of a number of possibilities, but the films themselves exclude many of them, such as a large parapelvic cyst, which might have calcification in its walls and might connect with the renal pelvis. The question of tuberculosis also comes up. Tuberculosis does occur in association with stones in a fair proportion of cases at the age of this patient. It would be unusual that nothing was found in the bladder to suggest tuberculosis.

We come next to the question of tumor within the kidney comprising the major bulk of the mass and causing nonfunction of that kidney. Tumors of the renal pelvis, particularly of the nonpapillary type, do occur in association with stones within the renal pelvis and probably more commonly than in kidneys without stones. This is comparable to the greater incidence of carcinoma of the gall bladder in association with gallstones than in the absence of stones. Tumor of the renal pelvis causing nearly complete obstruction at the ureteropelvic junction is therefore a good possibility, and it might explain the failure to get urine from the catheter, since the kidney may have been nonfunctioning.

Another excellent possibility in this case is perinephric abscess. It would fit in with a certain group of cases associated with renal calculi of long standing. I do not believe that the history of several months' duration is against the diagnosis of the chronic type of perinephric abscess. Renal stones occasionally erode through the pelvis and actually through the renal parenchyma to cause such abscesses. In my mind, the possibilities lie between a carcinoma of the renal pelvis and a perinephric abscess. I favor the former diagnosis: a nonpapillary, squamous-cell carcinoma of the renal pelvis, associated with stones.

FIGURE 3.

DR. BENJAMIN CASTLEMAN: What did you think about this, Dr. Colby?

DR. FLETCHER H. COLBY: That is exactly the diagnosis that I should have made.

### CLINICAL DIAGNOSES

Carcinoma of left kidney; perinephric abscess? Nephrolithiasis.

### DR. SIMEONE'S DIAGNOSES

Squamous-cell carcinoma of left renal pelvis. Nephrolithiasis.

### ANATOMICAL DIAGNOSES

*Squamous-cell carcinoma of left kidney, with extension into psoas muscle and with metastases to lung and liver.*

Nephrolithiasis, bilateral.
Duodenal ulcers, multiple (four).

### Pathological Discussion

Dr. Castleman: Dr. Leadbetter, will you describe the operative findings?

Dr. W. F. Leadbetter, Jr.: I operated with the expectation of finding either abscess or a degenerative tumor. It turned out to be the latter. It was a large mass that had extended behind and above the kidney, with involvement of the psoas muscle, and well into the connective tissue around the aorta. It was obviously a malignant tumor. I drained it, and there was a good deal of relief for some weeks.

Dr. Castleman: Autopsy showed a large tumor of the left kidney, which weighed about 1200 gm. The tumor, as Dr. Leadbetter has said, extended down into the psoas muscle and formed a fistula with the operative wound. The renal artery opened directly into the mass and was lost in it. The ureter was also imbedded in the mass and the proximal portion of the renal vein was filled with tumor. There was a stag-horn calculus, imbedded in a granular infiltrating tumor that originated in the pelvis (Fig. 3). Microscopically, it was a squamous-cell carcinoma. The other kidney also contained calculi, and these were floating in foul green pus. There was one small metastasis to the right lung and a few small ones to the liver.

An incidental finding — and it is amazing that the patient had no symptoms from it — was the presence of four large duodenal ulcers, two in the first portion of the duodenum and two in the second portion, one of which extended to the ampulla of Vater. One had eroded into the pancreas, and another, the most proximal, formed a fistula with the neck of the gall bladder.

Dr. Isaac Taylor: Were the ulcers old?

Dr. Castleman: No; fairly recent.

## CASE 33472

### Presentation of Case

*First admission.* A seventy-six-year-old man entered the hospital complaining of intermittent periumbilical and left abdominal nonradiating pain of two months' duration.

The patient stated that the pain was dull "like a toothache" and located along a transverse area at the level of the umbilicus, primarily on the left side. There was no known predisposing factor, and there was no change in bowel habits, or melena. Vomiting occasionally resulted in relief of pain. At a community hospital the patient was told that he had jaundice although he had no itching or dark urine. X-ray studies at the hospital were said to have shown a possible neoplasm of the pancreas. During the preceding three months he had felt weak and tired and had an "all-gone" feeling.

Physical examination showed a well nourished man with a Grade II apical systolic murmur. A left direct inguinal hernia was present; abdominal examination was otherwise negative.

The temperature, pulse and respirations were normal. The blood pressure was 130 systolic, 90 diastolic.

Examination of the blood disclosed a hemoglobin of 14.5 gm. and a white-cell count of 10,000. The urine showed a 0 to + test for albumin, with a specific gravity of 1.020, and 6 to 20 white cells per high-power field in the sediment. The nonprotein nitrogen was 26 mg. per 100 cc., the protein 7.4 gm., and the chloride 100 milliequiv. per liter. The prothrombin time was normal. A barium enema showed a few diverticulums of the sigmoid but was otherwise not remarkable. An intravenous pyelogram and chest film revealed no significant abnormalities. A gastrointestinal series disclosed prominent lesser-curvature folds in the prepyloric area. The duodenum was deformed, and barium entered the biliary tree.

A sigmoidoscopy was negative. The hernia, which was indirect and contained adherent sigmoid posteriorly, was repaired. The patient did well postoperatively and was discharged four days later.

*Second admission* (six weeks later). The patient was readmitted because the midabdominal left-lower-quadrant pain had persisted, occurring several times a week, and had been accompanied by vomiting. Twice he had been jaundiced for about a week and had pale stools. Weakness, fatigue and anorexia had appeared. At times a brief "pressing, clamped feeling" had been noted across the epigastrium.

Physical examination was essentially as before. The herniorrhaphy incision was well healed.

A second gastrointestinal series showed the same findings in addition to a duodenal diverticulum. A cholecystogram revealed no filling of the gall bladder. Gastric aspiration demonstrated a + guaiac reaction and no free acid. The white-cell count was 13,600. The urine was normal, except for 30 to 40 white cells per high-power field in the sediment.

The blood chemical findings were normal, including a van den Bergh reaction. A serum amylase test was 7 units per 100 cc.

On the eleventh hospital day a cholecystectomy and choledochostomy were performed. The gall bladder was a mass of scar tissue, with the duodenum drawn up in the scar. The common duct was markedly dilated and contained stones and muddy material. No definite fistula was demonstrated. Postoperatively the systolic blood pressure was between 70 and 80 for seven hours. Two blood transfusions were given, with a gradual rise in blood pressure. Mild congestive failure was treated with digitalization. Prophylactic femoral-vein ligations were performed. On the fourteenth postoperative day the patient was discharged after a cholangiogram showed patent ducts.

*Final admission* (nineteen days later). Several days after discharge the patient began to vomit three or four times a day. Bile-stained material drained from the operative wound, but the stools remained brown and he was readmitted for study.

Physical examination showed a frail, dehydrated, uncomfortable man with a normal temperature. The lungs were clear and the diaphragm moved equally on both sides. The transverse right upper abdominal incision was indurated laterally, and pus and bile exuded from a sinus.

The white-cell count was 12,800. The urine was essentially normal. The nonprotein nitrogen was 41 mg. and the protein 5.5 gm. per 100 cc., and the chloride 80 milliequiv. per liter. The prothrombin time was 22 seconds, with a control of 17 seconds. A van den Bergh reaction was normal, and the serum amylase was 48 units per 100 cc. Injection of the sinus tract showed a dilated obstructed common duct. A gastrointestinal series revealed thick antral folds but no duodenal defects.

A transduodenal choledochostomy about two weeks after admission disclosed no obstruction, but a pericholedochous abscess was encountered. A duodenal choledochal fistula was present. Postoperatively, the patient did well for a few days but then gradually went downhill. He vomited frequently, the vomitus being guaiac positive. X-ray films showed a narrow nonobstructed duodenum. The pylorus and duodenal loop could not be visualized. While barium was still in the duodenal loop Hippuran injection through the "T" tube revealed a considerably distended common duct, with some pooling near it. There was no certainty that the Hippuran passed through the duodenal loop and small intestine. The main radicle leading to the left lobe of the liver showed a constant, round, filling defect consistent with a retained common-duct stone. The nonprotein nitrogen rose to 96 mg. per 100 cc., and the urine output fell. The white-cell count rose to 30,000. On the fourteenth postoperative day the patient fell out of bed and went into shock. He was treated with two transfusions, after which he rallied but gradually lost ground again, developing an irregular pulse and coma. He died four days later.

## Differential Diagnosis

Dr. Francis D. Moore: This patient had had so much surgery and so many events on various admissions that the modus operandi today will be to follow the same order as that in which he was presented to his physician.

In the first place, he looked well enough at one point so that someone wanted to repair the hernia. He could not have appeared seriously ill. I wonder how much of the story was extracted in retrospect.

He had pain "like a toothache," which has a little significance, meaning probably that it was not smooth-muscle pain or pain resulting from colic, but was more likely pain due to a space-occupying process, which could be either a neoplasm or sepsis. This was located in an area to the left of the umbilicus, which certainly suggests the pancreas. Furthermore, he had been told at another hospital that he had jaundice, although he had no itching or dark urine, and I am inclined to believe that the scleras were examined and that slight jaundice was noticed. X-ray studies at that hospital apparently showed something in the region of the pancreas. The patient had an "all-gone" feeling. In other words, he was beginning to have a systemic response to the process, whatever it was.

Then the left inguinal hernia was repaired. At these meetings it is easy to be too critical of what others have done. There is nearly always a good reason, although it may not be apparent. However, we should learn from the warning given in this case that hernias are sometimes misleading. Many patients with a hernia in the inguinal region that has been present for years suddenly experience trouble and come to the doctor. The reason is usually not found in the hernia. There is some other intra-abdominal process causing increased pressure or irritating the peritoneum, which makes the patient notice the hernia. In older people a complete study, prior to herniorrhaphy, is certainly justified. I imagine that the various x-ray films were taken, because the physicians were disturbed about repairing a hernia in this elderly man who had other evidences of disease. It was noted that barium entered the biliary tree — a finding that to my knowledge always coexists with structural disease in that area; I am interested in seeing the film.

Dr. Toufic Kalil: It was probably a fluoroscopic finding. I do not see it recorded.

Dr. Moore: If the fluoroscopist saw barium entering the biliary tree, that is significant, even if the films are not spectacular. The most frequent cause of air entering the biliary tree is a cholecystduodenal fistula, which results from a gallstone eroding through into the duodenum. It can also erode through the common duct, and a cholecystocolic fistula can form in the same way and produce the same picture. I have not happened to see other nonsurgical conditions cause it. Of course, surgical maneuvers can produce that picture. The duodenal diverticulum that was demonstrated is not the primary lesion, and its significance as a cause of symptoms or of difficulty of any sort is usually regarded as slight. In any event, in the face of gross roentgenologic evidence of disease around the lower end of the biliary tree, this patient had his hernia repaired and was discharged four days later, which seems to me too early for discharge. Is that correct?

Dr. John W. Raker: That is correct.

Dr. Moore: The patient had a history that was consistent with pancreatic complications. He had x-ray evidence of gross organic disease, with de-

struction of the normal anatomy. At the second admission this process was continuing its inexorable advance, he had been jaundiced, had pale stools and was having intermittent common-duct obstruction. Other symptoms of a systemic nature were present.

The second gastrointestinal series again showed the diverticulum. There was no filling of the gall bladder with a cholecystogram. Without further information it is hard to know whether that is significant; it probably indicates chronic inflammation of the gall bladder. The white-cell count was elevated, indicating a septic process; the urinary sediment showed white cells. The blood chemical levels were generally normal, and included a serum amylase of 7 units per 100 cc. To my way of thinking, that is an unusually low serum amylase, and possibly indicates that the acinar cells of the pancreas were not functioning normally. One sees that occasionally in late chronic pancreatitis, or in neoplasms of the head of the pancreas with chronically obstructed ducts. The serum amylase later went back up to 48 units per 100 cc., and I do not know how to interpret that; possibly extrapancreatic sources of serum amylase were responsible.

On the eleventh day an operation was performed. Before going on, let us see again if we get any help from x-ray studies done on the second admission.

Dr. Kalil: These films demonstrate the Hippuran injections through the postoperative tube.

Dr. Moore: I do not know what the preoperative diagnosis was. But I think in terms of smoldering chronic pancreatitis superimposed on cholelithiasis and cholecystitis — a combination not too unusual. What was found was a gall bladder showing evidences of cholelithiasis. The duodenum was drawn up to the scarred common duct, which was dilated and contained stones and muddy material. In other words, the caliber of the cystic duct was such as to allow gallstones to pass into the common duct, producing obstruction enough to cause secondary pancreatitis. There was no fistula demonstrated, which is not surprising; it is often difficult to find. I should like to ask Dr. Mallory if any note was made at any time regarding the appearance and feel of the pancreas.

Dr. Tracy B. Mallory: No; there were too many adhesions in the area.

Dr. Moore: Femoral-vein ligation was done to keep the patient from dying of pulmonary embolism. A cholangiogram was carried out, and the patient was discharged. Let us see the films of the cholangiogram.

Dr. Kalil: This is the patent common duct, with the T tube in it.

Dr. Moore: The third admission occurred very soon, only nineteen days later. The patient had lost a good deal of ground systemically, and much bile had seeped through the wound. There is no mention that the tube was still in place.

The normal temperature is interesting. It possibly had something to do with the patient's age, because there was an elevated white-cell count and considerable sepsis was found a few days later. He had dehydration, as evidenced by the chemical determinations — a low chloride and a protein of 5.5 gm. per 100 cc. It is fair to assume that he had been rehydrated and that the protein went down as a result. The van den Bergh reaction was normal, which is puzzling, but we shall see in a moment a possible explanation for that. The serum amylase was 48 units per 100 cc. — back to the normal range.

Injections of the sinus tract showed a dilated, obstructed common duct. I think that this was the film showing the obstruction on the distal end.

Dr. Kalil: It is a very abrupt ending of the opaque column, rather smoothly rounded, and the material filters down on both sides.

Dr. Moore: The common duct is 2 cm. in diameter. There is something in the lower end, which could be a stone, but if it is a stone, it is a tremendous one. It could well be a tumor mass.

A transduodenal choledochostomy was done, presumably because of the lesion in the lower end, but nothing was found. That was a surprise. A pericholedochous abscess was encountered. There was still sepsis, and the duodenocholedochal fistula was present. The original fistula was finally located and was not cholecystduodenal but choledochoduodenal. This accounted for the barium in the biliary tree seen on the first films.

The operation did not relieve the fundamental disease, and the patient finally died. Before death one more Hippuran injection demonstrated that the main radicle in the left lobe of the liver showed a filling defect consistent with stone. We do not know what the pancreas felt like at the third operation — it was probably impossible to feel it because of obliteration of normal structures.

The patient seemed to be suffering from liver failure. The white-cell count rose to 30,000. On the fourteenth postoperative day he suffered a minor trauma and finally died.

From the systemic point of view I believe that this patient had sepsis, nutritional depletion, dehydration and liver failure. Did he have some fundamental process, such as carcinoma, that was causing the entire picture? He could have had a carcinoma of the pancreas; I somehow believe that more concrete evidence would have been found in two surgical attempts in the right upper quadrant. If all this is blamed on carcinoma of the pancreas, it must be concluded that the obstruction to the duct was on that basis, and yet this was not so at operation.

Could the patient have had lymphoma or some other bizarre neoplastic process masking the sepsis? Reticulum-cell sarcoma often acts in that way, but such a diagnosis would be just a guess because we have no histologic evidence. There was an element of congestive failure. Terminally, I think that he

had cholemia, the clinical syndrome of liver failure, which can co-exist with a surprisingly low serum bilirubin, which in this patient seemed to be normal most of the time; but we must not forget that one lobe may have been obstructed while the other drained reasonably well.

What else could have caused the gradual downhill course? I cannot help thinking in terms of liver abscess. This patient had sepsis. We have no culture, but it may have been a virulent organism that was floating up and down the extrahepatic biliary tree for many months. The drainage was not adequate, and although liver abscess is much more commonly a blood-borne than a duct-borne lesion, I think that in this exceptional case, in which there was so much sepsis in and around the duct and evidence of at least anatomic obstruction of the duct, he may have had an abscess in the left lobe of the liver. If so, it would be less likely to show as a distortion of the diaphragm by x-ray study, because the left lobe of the liver is under the mediastinum instead of being under the free diaphragmatic structures.

My final diagnosis is heart disease, which I assume was arteriosclerotic in nature, with congestive failure, cholemia, sepsis around the common duct and liver abscess.

Dr. Raker: One thing might be said about the hernial repair. The gastrointestinal series was originally interpreted as normal. The hernia was repaired, and it was not until after discharge that the final report came back showing this fistula.

Dr. Moore: That is important. Such a delay happens all too frequently, simply because of a slow rapport between the services.

Dr. F. Dennette Adams: Why did you give up the thought — or rather why did you not concentrate on the thought — that the pancreas was involved as the result of chronic infection?

Dr. Moore: One reason was that an amylase of 7 units per 100 cc. was recorded, and the level went back up to 48 units within a few weeks. It makes it seem unlikely to me that a great deal of acinar tissue had been destroyed. There is no question that there was inflammation in the pancreas, but I doubt if a pancreatitis was the cause of the whole disorder. I have already mentioned my reasons for believing that although carcinoma of the pancreas was possible, it was an unlikely cause for the whole picture.

### Clinical Diagnoses

Spreading peritoneal sepsis.
Cholecystitis, with cholelithiasis, postoperative.
Uremia.

### Dr. Moore's Diagnoses

Arteriosclerotic heart disease, with congestive failure.
Cholemia.
Chronic cholangitis.
Liver abscess.

### Anatomical Diagnoses

*Adenocarcinoma of body of pancreas, with extension into and ulceration of stomach.*
Choledochoduodenal cutaneous fistula.
Pericholedochal abscess.
Peritonitis, localized.
Pneumonitis, aspiration type, bilateral.
Diverticulum of duodenum.
Diverticulitis and diverticulosis of sigmoid.
Operations: cholecystectomy, old; choledochostomy, recent and old; left inguinal herniorrhaphy, old; bilateral, superficial femoral-vein ligations, old.

### Pathological Discussion

Dr. Mallory: The findings at autopsy were complicated. There were many adhesions throughout the abdomen, particularly around the region of the common duct and duodenum, and I am sure that that is what prevented exploration of the pancreas. There had been an acute sepsis about the common duct, which had been pretty well cleared up by the last operation. We did find one pocket of retroperitoneal pus above the upper pole of the right kidney and between the liver and kidney. That was relatively small, measuring 2.5 cm. in diameter. The fistula between the duodenum and the common duct was still present, and the ampulla was apparently perfectly patent, admitting a probe without difficulty. There was therefore no demonstrable obstruction of the biliary tract at the time of autopsy.

The heart showed a moderate grade of calcareous aortic stenosis, with considerable interadherence of the cusps and marked calcification, which would have prevented their complete opening.

The surprise of the autopsy was a large area of ulceration on the lesser curvature of the stomach, 4.5 cm. in one diameter and 3 cm. in the other. There was no suggestion of it in any of the x-ray studies. This was a deep ulcer, and the bed of the ulcer was formed by the pancreas. The pancreas seemed rather firm throughout but presented no areas of necrosis and no gross appearance of tumor. It was thought to be a chronic pancreatitis secondary to a penetrating gastric ulcer. When, however, we came to examine the microscopical sections, we were forced to change our minds drastically. Diffusely infiltrating through the pancreas was an adenocarcinoma, and the stomach was obviously secondarily involved by a cancer that was primary in the pancreas.

Dr. Moore: It helps to demonstrate the truth of the old adage that if we lean too heavily on any one diagnostic aid — in this case x-ray examination — it may give way and let us down hard.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
and
THE NEW HAMPSHIRE MEDICAL SOCIETY

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SUBSCRIPTION TERMS: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.00 per year (Boston funds); $8.50 per year for all foreign countries belonging to the Postal Union.

MATERIAL should be received not later than noon on Thursday, three weeks before date of publication.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

## THANKSGIVING

IT HAS become a pleasant custom of the editorial writers of the *Journal* to comment on the annual return of certain significant holidays, and to recall what comfort or inspiration may be found in the occasion. The observance of Thanksgiving Day is particularly appropriate to this custom, for we think of our Thanksgiving, although a national holiday, as belonging especially to New England, where its celebration originated.

In 1621, after the first harvest of the Pilgrim Fathers had been gathered, Governor Bradford appointed a day of thanksgiving and prayer for the event. In 1623, during one of those extended droughts with which every New England farmer is familiar, a day of fasting and prayer was changed into one of thanksgiving for the rain that fell even during the prayers that were raised in suppliance for it. The Lord had let the light of His countenance shine upon the New World.

Soon all the New England colonies, by proclamation of their several governors, were observing a day of thanksgiving after their crops had been harvested and stored. The custom spread from New England. A Thanksgiving Day was annually recommended by the Continental Congress during the Revolution, and in 1864 President Lincoln inaugurated the custom, followed by each succeeding president, of proclaiming a general day of Thanksgiving for all the land.

Despite our tendency in this country to think of Thanksgiving as a uniquely American holiday (given to the rest of the nation by New England) there is no particular reason for cherishing a belief that the expression of gratitude, even to a higher power, had its origin in the Western Hemisphere. Noah, we are told, many years before the appearance of that other bold navigator, Columbus, erected an altar after his deliverance from the flood and offered thereon "of every clean beast and every clean fowl burnt offerings unto the Lord in Thanksgiving." The English, in November, 1588, thirty-two years before the Pilgrims set foot on Plymouth Rock, held their own first official Thanksgiving for the defeat of the Spanish Armada, with Queen Elizabeth in attendance.

So we too may recapitulate those facts for which we have reason to be thankful, but differing from the Pharisee who thanked God that he was not as other men nor even as the publican, preoccupied with his own humility. We may be thankful for that basic principle of equality that we recognize and cherish. We may be thankful that out of our abundance we are able and minded to help those from whom so much has been taken — that we, as physicians, are privileged for a while to carry the torch of learning and with it to kindle new fires in some of the lands where the light has come so close to extinction.

Let us be thankful at this season, not only for our possessions but for the desire to share them, not alone for security but for the courage to maintain it!

## STUDY OF THE RUBELLA SYNDROME

AN AMAZING fact in the annals of modern medicine is the recent discovery of the relation between maternal rubella and the occurrence of certain congenital defects in the fetus. Apparently unheard of less than a decade ago, it has, in a surprisingly short time, become common knowledge that infection of a mother with rubella in the first trimester of pregnancy will result, in a large percentage of cases, in the occurrence of such defects as cataracts, deafness, microcephaly, mental deficiency and congenital heart disease in the fetus.

Such sinister sequelae from a virus infection so benign as rubella is generally considered to be are disturbing; they serve to increase still further our growing respect for virus diseases in general, and their possible late effects. Why this particular train of events has been hidden so long is a matter of conjecture. The relative infrequency of rubella and its usually mild manifestations in the age group involved, as well as the time interval between cause and effect, are probable factors.

More information is necessary before we have a clear picture of the effects of virus infection in the early months of pregnancy. Additional cases must be studied in which congenital malformations in the fetus have followed rubella in the mother; of particular importance will be figures on the incidence of rubella in early pregnancy *without* fetal complications, and a searching analysis of other types of virus disease to determine if they, too, may be involved in such a catastrophic sequence.

To this end a year's study has been launched and financed by the National Society for the Prevention of Blindness, Inc., with the approval of the American Academy of Pediatrics, and questionnaires are being sent to obstetricians, ophthalmologists and pediatricians, seeking pertinent information on the subject. Data will be collected on four types of cases: children with congenital defects associated with rubella in the mother during pregnancy; children without congenital defects whose mothers had rubella during pregnancy; children with congenital defects associated with other maternal infections in the first trimester of pregnancy; and children with the so-called "rubella syndrome" (cataracts, deafness, microcephaly and congenital heart disease) unassociated with any maternal infection during pregnancy.

The occurrence of any such cases should be reported to Dr. Herbert C. Miller, University of Kansas Hospitals, Kansas City, Kansas, the chairman of the committee entrusted with the study.

## MASSACHUSETTS MEDICAL SOCIETY

### DEATHS

BAUM — Ewald G. Baum, M.D., of Natick, died on October 22. He was in his sixty-third year.

Dr. Baum received his degree from George Washington University School of Medicine in 1911. He was the inventor of a milk-bottle cap to protect bottle tops from contamination. He was a fellow of the American Medical Association.

His widow, two stepchildren, a sister, two brothers and a nephew survive.

KING — Frederick A. King, M.D., of Marshfield, died on September 14. He was in his seventy-ninth year.

Dr. King received his degree from Boston University School of Medicine in 1895.

Two sons survive.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### MASSACHUSETTS STATE PLAN

The acute need for additional hospital facilities in this country resulted in 1946 in the enactment of Public Law 725, the Hospital Survey and Construction Act, by the Seventy-Ninth Congress. This act establishes a grant-in-aid program to assist the states to plan and build additional hospital and health-center facilities where they are most needed. In the next five years, under this program, total expenditures in Massachusetts alone will amount to twenty-four millions. Of this amount, a third will be allotted by the federal government and two thirds will come from state or local sources.

The Massachusetts plan for the administration of Public Law 725 is being developed in several stages. The first step consists of a survey of all existing hospitals and health-center facilities in the Commonwealth. After completion of the survey, the Commonwealth is divided into three categories of general hospital service areas designed as base, intermediate and rural, depending on population and the existing or proposed general-hospital facilities within the area. The next step is the determination of general bed needs by formulas established by the United States Public Health Service for each type of area that leads to the establishment of a priority schedule. The order of general-hospital projects built under this act must conform with this priority scheme. Finally, consideration is given to the determination of needs in the other categories of facilities — that is, tuberculosis, mental and chronic disease hospitals and public-health centers

—by standards established by the United States Public Health Service.

After approval of this plan by the State Advisory Council and the Surgeon General of the United States Public Health Service, a construction program will be developed for a five-year period in which federal funds will be distributed among the five categories of facilities mentioned above.

## COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1947

### Résumé

| Diseases | September 1947 | September 1946 | Seven-Year Median |
|---|---|---|---|
| Chancroid | 2 | 1 | 1* |
| Chicken pox | 123 | 110 | 106 |
| Diphtheria | 10 | 50 | 10 |
| Dog bite | 960 | 1079 | 924 |
| Dysentery, bacillary | 14 | 5 | 17 |
| German measles | 43 | 56 | 49 |
| Gonorrhea | 393 | 443 | 410 |
| Granuloma inguinale | 0 | 0 | 0* |
| Lymphogranuloma venereum | 0 | 1 | 1* |
| Malaria | 7 | 25 | 13 |
| Measles | 69 | 204 | 168 |
| Meningitis, meningococcal | 3 | 8 | 8 |
| Meningitis, Pfeiffer-bacillus | 0 | 2 | 0 |
| Meningitis, pneumococcal | 1 | 3 | 1† |
| Meningitis, staphylococcal | 0 | 0 | 0† |
| Meningitis, streptococcal | 1 | 1 | 0† |
| Meningitis, other forms | 1 | 0 | 1† |
| Meningitis, undetermined | 10 | 1 | 2† |
| Mumps | 148 | 101 | 194 |
| Pneumonia, lobar | 31 | 37 | 106 |
| Poliomyelitis | 149 | 100 | 100 |
| Salmonellosis | 25 | 20 | 13 |
| Scarlet fever | 130 | 138 | 241 |
| Syphilis | 206 | 352 | 363 |
| Tuberculosis, pulmonary | 217 | 237 | 229 |
| Tuberculosis, other forms | 16 | 19 | 19 |
| Typhoid fever | 1 | 3 | 3 |
| Undulant fever | 10 | 1 | 2 |
| Whooping cough | 646 | 520 | 520 |

*Three-year median.
†Five-year median.

### Comment

Diseases above the seven-year median were chicken pox, dog bite, poliomyelitis, salmonellosis, undulant fever and whooping cough.

Diseases below the seven-year median were bacillary dysentery, German measles, gonorrhea, malaria, measles, meningococcal meningitis, mumps, lobar pneumonia, scarlet fever, syphilis, tuberculosis and typhoid fever.

The downward trend of diphtheria has continued since June, 1947, so that it is now at the seven-year median. It is unlikely that this low prevalence will be maintained unless more energetic immunization programs are carried on.

Poliomyelitis is the highest recorded for the year — an incidence of 149 cases in September compared to 80 in August and 21 in July. The peak for the season appears to have been reached.

There is an indication that the upward trend in whooping cough, which had halted during the summer, is being resumed.

### Geographical Distribution of Certain Diseases

Diphtheria was reported from: Ashburnham, 1; Bolton, 1; Boston, 7; Westfield, 1; total, 10.

Dysentery, bacillary, was reported from: Boston, 1; Lexington (Metropolitan State Hospital), 6; Malden, 2; Salem, 2; Worcester, 1; Wrentham (State School), 2; total, 14.

Encephalitis, infectious, was reported from: Salisbury, 1; Quincy, 1; Wareham, 1; total, 3.

Malaria was reported from: Boston, 2; Braintree, 1; Everett, 1; Malden, 1; Seekonk, 1; Worcester, 1; total, 7.

Meningitis, meningococcal, was reported from: Fall River, 1; Lowell, 1; Wellesley, 1; total, 3.

Meningitis, pneumococcal, was reported from: Melrose, 1; total, 1.

Meningitis, streptococcal, was reported from: Taunton, 1; total, 1.

Meningitis, other forms, was reported from: Amesbury, 1; total, 1.

Meningitis, undetermined, was reported from: Fall River, 1; Middleboro, 1; Newton, 1; North Attleboro, 1; Norwood, 1; Pittsfield, 2; Sheffield, 1; Wareham, 1; Wrentham, 1; total, 10.

Poliomyelitis was reported from: Andover, 1; Arlington, 3; Athol, 1; Barnstable, 1; Becket, 1; Bellingham, 1; Beverly, 1; Boston, 23; Braintree, 1; Bridgewater, 1; Brockton, 2; Brookline, 9; Cambridge, 5; Canton, 1; Concord, 2; Dartmouth, 2; Dedham, 4; Egremont, 1; Everett, 1; Fall River, 7; Freetown, 1; Greenfield, 1; Hingham, 3; Lowell, 1; Lynn, 6; Marshfield, 1; Medford, 2; Middleboro, 2; Milton, 5; Natick, 2; New Bedford, 2; New Marlboro, 2; Newton, 5; North Brookfield, 1; Quincy, 2; Reading, 2; Revere, 1; Salem, 1; Saugus, 1; Sheffield, 2; Somerset, 1; Somerville, 2; Southbridge, 1; Springfield, 2; Sudbury, 3; Taunton, 3; Templeton, 1; Tewksbury, 1; Wakefield, 1; Waltham, 3; Watertown, 1; Wayland, 1; Wellesley, 2; West Bridgewater, 1; West Springfield, 1; Westport, 1; Weymouth, 1; Winchendon, 1; Winthrop, 1; Worcester, 10; total, 149.

Salmonellosis was reported from: Andover, 1; Attleboro, 1; Boston, 2; East Bridgewater, 1; Gloucester, 1; Holyoke, 4; Lawrence, 1; Lowell, 3; Lynn, 1; Marblehead, 1; Medford, 3; Monterey, 1; Newburyport, 1; Salem, 2; Saugus, 1; Templeton, 1; total, 25.

Septic sore throat was reported from: Amesbury, 1; Boston, 3; Haverhill, 1; Quincy, 1; total, 6.

Tetanus was reported from: Brockton, 1; Great Barrington, 1; total, 2.

Trachoma was reported from: Wakefield, 1; total, 1.

Trichinosis was reported from: Boston, 1; Fall River, 2; Falmouth, 1; total, 4.

Typhoid fever was reported from: Shrewsbury, 1; total, 1.

Undulant fever was reported from: Bedford, 1; Belchertown, 1; Fitchburg, 1; Greenfield, 1; Holyoke, 1; Mansfield, 1; Palmer, 1; Somerset, 1; Warren, 1; Weston, 1; total, 10.

## CORRESPONDENCE

### NATIONAL PHYSICIANS COMMITTEE

*To the Editor:* A recent communication from the National Physicians Committee entitled "Factual Memorandum" says, "The source of the unremitting and relentless drive for Compulsory Health Insurance — Socialized Medicine — the Political Distribution of Medical Care in this country — is the Moscow dominated Communist Party of the United States."

The facts in regard to attempts to develop a National Health Program to be financed by compulsory health insurance are as follows: In 1938 President Franklin D. Roosevelt called a National Health Conference in Washington following which the first Wagner–Murray–Dingell Bill for Compulsory Health Insurance was introduced in 1939. This was followed by similar bills introduced by the same gentlemen in 1943 and 1945. On November 19, 1945, President Harry S. Truman requested legislation for adoption of a National Health Program, and at the same time Senators Wagner and Murray and Representative Dingell introduced a fourth bill entitled The National Health Act of 1945. Hearings were held on this bill before the Senate Committee on Education and Labor in the Spring of 1946, during the course of which Senator Taft supported by the American Medical Association and the National Physicians Committee introduced a bill entitled The National Health Act of 1946. Finally in the present Congress there are two health bills, one introduced by Senators Taft, Smith, Ball and Donnell in February, 1947, entitled The National Health Act of 1947, S. 545, and the other by Senators Murray, Wagner, Pepper, Chavez, Taylor and McGrath in May, 1947, entitled The National Health Insurance and Public Health Act of 1947, S. 1320. Thus it becomes apparent that both political parties now favor a National Health Program of some sort, and the question is, What will be the best program?

Both these bills of course are equally compulsory: the former requiring compulsory contributions to general taxes, and the other compulsory payroll contributions. Neither bill is compulsory as regards the receipt or the giving of medical services.

The main difference between the two bills is that the one favors the raising of the major part of the funds by the insurance principle from employed people and only using general tax funds to cover the needs of the unemployed. This eliminates the problem of administering a costly means

test. It provides that the majority of people will be paying for their care and not getting free medicine. The other bill calls for the delivery of medical care paid for by taxes as charity after a means test has established the individual's eligibility. This means the recipients will be getting free care. As medical care is bound to become more expensive, this program will almost inevitably include an ever-increasing proportion of the population. Even today fifty per cent of the people would probably claim and qualify for eligibility for part of their medical care. Thus the Taft Bill is just as much "Socialized Medicine" as the Wagner Bill. Indeed Ex-Governor Arnall characterizes it as Bismarckian state socialism of the most paternal type.

The idea of a National Health Program financed by Compulsory Health Insurance which was originated by President Franklin D. Roosevelt and furthered by President Harry S. Truman is now openly supported among others by the following groups of our citizens: American Association of Social Workers; Americans for Democratic Action; American Federation of Labor; American Veterans Committee; Congress of Industrial Organizations; Cooperative League of the United States of America; Council for Social Action of the Congregational Christian Churches; Methodist Federation for Social Service; National Association for the Advancement of Colored People; National Federation of Settlements; National Catholic Welfare Conference; National Consumers League; National Council of Jewish Women; National Council of Negro Women; National Farmers Union; Committee for the Nation's Health, Inc.; Committee of Physicians for the Improvement of Medical Care, Inc.; and The Physicians Forum, Inc.

It must seem absurd to any intelligent person that two presidents of the United States and the above groups could be under the control of the Moscow-dominated Communist Party of America. It is hard for me to believe that the National Physicians Committee honestly thinks so. Therefore, I am forced to the conclusion that this Committee is either grossly ignorant of the facts or actually trying to misinform the medical profession. This suspicion that the National Physicians Committee, whose actions have been approved by the House of Delegates of the American Medical Association, knowingly circulates misinformation is strengthened by its actions in the past.

In the publications of the hearings before the Committee on Education and Labor, United States Senate, 79th Congress, Second Session on S. 1606, Part 5, page 2679, seven quotations from the literature circulated by the National Physicians Committee are included, and in each instance are proved false by quotations from the *Journal of the American Medical Association*. An example follows: Misstatement by the National Physicians Committee: "The doctor would have little if any interest in the patient who is compelled to visit him." Refutation by quotation from the *Journal of the American Medical Association*, "A patient may select any doctor." The other six misstatements recorded are as simply refuted by the *Journal of the American Medical Association* as the above. It is of interest that no denial of the accuracy of these senatorial records showing the falsity of statements by the National Physicians Committee has been forthcoming.

If the medical profession of this country wishes to form an honest opinion in regard to the relative value of the National Health Program under discussion, it seems only fair that it should be permitted to judge the issue from statements of fact rather than from misrepresentations broadcast by the National Physicians Committee. Yet the tragic truth is that in the medical journals throughout the country with the exception of the *New England Journal of Medicine* and the *Official Journal of the American Academy of Pediatrics* little if any opportunity is offered for presentation of opinions other than those of the House of Delegates of the American Medical Association.

Physicians should be alert not to be deceived about the actual facts of proposed National Health Programs by the false statements of the National Physicians Committee. The subject is of vital importance to physicians. It deserves serious consideration, not prejudiced propaganda.

CHANNING FROTHINGHAM, M.D.

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## BOOK REVIEWS

*The Development of Inhalation Anesthesia: With special reference to the years 1846–1900.* By Barbara M. Duncum, D.Phil. (Oxon.). Publications of the Wellcome Historical Medical Museum. 8°, cloth, with 161 illustrations. New York: Oxford University Press, 1947. $12.00.

The centennial of ether anesthesia in 1946 led to the publication last year of several commemorative and historical volumes, such as Dr. Rapar's *Man Against Pain*, Dr. Robinson's *Victory over Pain* and the authentic, monumental work by the reference librarian for the Mayo Clinic. In sequence to these the present volume, second in the new series of publications by the Wellcome Historical Medical Museum, is an official British history of the development of anesthesia. The author, as a member of the Nuffield Department of Anaesthesia of the University of Oxford, had unusual opportunity of research for this study, and has attempted not merely "to trace the beginnings and to follow the development of those concepts and practices which have gone to the making of the science and art of inhalation anaesthesia," but also "to show how current beliefs and happenings affected its evolution." The volume is well illustrated with a hundred and sixty-one engravings, presents a number of special topics in a series of five appendixes and closes with a chronologic summary of events in the history of anesthesia from Priestley's discovery of nitrous oxide in 1772 to Levy's study in 1911 of ventricular fibrillation under chloroform. Dr. Duncum writes with authoritative scholarship. She has made a distinguished and valuable contribution to medical history.

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*The Psychoanalytic Study of the Child.* Volume II. 8°, cloth, 424 pp. New York: International Universities Press, 1947. $7.50.

This book is a collection of papers, some original and some revised, on a wide variety of topics in psychoanalysis. The factual data concerning psychoanalytic findings and therapy in children or adolescents are meager in proportion to the quantity of strictly nonpediatric discussions and formulations. If the reader is to believe that in the book was gathered material for bringing up to date the workers in psychiatry and related fields in child psychoanalysis, the bibliographies at the end of each chapter (each presentation) are for the most part rather old. This gives the impression that each author has picked on a highly specialized topic on which to expound. Each paper is set apart from the others, making the book uncohesive, and many items are repeated. Some discussions are polemic — for example, that on page 324, in which barbs are thrust at Klein, Adler, Jung and others.

The case reports were unusually well written, interesting and instructive. They illustrated the necessary titled features quite closely.

Although some of the material is new, much of the matter discussed has previously been presented in the periodic literature and standard texts concerning psychoanalysis. To the reviewer the book appeared to be an oversized journal emphasizing by implication certain features of child and adolescent psychiatry.

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*The Postnatal Development of the Human Cerebral Cortex.* By J. LeRoy Conel, M.D. Cambridge, Massachusetts: Harvard University Press. Volume I (1939): *The Cortex of the Newborn.* F°, cloth, 106 pp., with 2 tables and 194 illustrations. $8.00. Volume II (1941): *The Cortex of the One-Month Infant.* F°, cloth, 136 pp., with 3 tables and 220 illustrations. $8.00. Volume III (1947): *The Cortex of the Three-Month Infant.* F°, cloth, 148 pp., with 6 tables and 219 illustrations. $12.50.

The first three volumes of this monumental contribution by Dr. Conel on the postnatal development of the human cerebral cortex, begun in 1939, have been published by the Harvard University Press. The printing of these studies was made possible by a grant from The John and Mary R. Markle Foundation, as well as by contributions from various research funds. The work has been conducted at Boston University School of Medicine, Harvard Medical School and the Children's and Infants' hospitals in Boston.

Dr. Conel plans a survey of the development of nerve cells in the normal human cerebral cortex for the purpose of observing what changes occur in the morphology of the neurons as development of the growing child proceeds. The investigations have been carried on meticulously. Autopsies were performed within twenty-four hours, the brains having been injected by formaldehyde through the common carotid artery, prior to removal. After suspension for a few days in a 10 per cent neutral formaldehyde solution the brains were cut. Paraffin sections were stained with cresyl violet, and celloidin section with the Golgi–Cox mercuric chloride method and the Cajal sulfur impregnation. Photographic sections, as well as camera lucida drawings of individual cells, are reproduced in the excellent plates. The characteristics of both the gross and the microscopical appearance of the cortex are given in detail, and a summary appears at the end of the second and third volumes indicating the changes found in the nerve tissue as compared with the basic findings on the brain of the newborn. The general pattern of the architectonics of the cerebral cortex in the brain of the three-month-old infant was found to be the same as that in the brain at the age of one month. There were, however, changes in microscopical structure corresponding to growth. The criteria used for comparison among others were the width of the entire cortex and of each horizontal layer, number of nerve cells, size of the cells, the condition of the chromophil substance, neurofibrils and the study of the myelinization. Most of the changes found in the first three months were in the fifth and sixth cell layers, with some changes in the lower parts of the third and fourth layers.

It is hoped that this fundamental survey will be continued and that adequate support for publication will be forthcoming. The work is an outstanding achievement. Special attention should be called to the fine presswork.

## BOOKS RECEIVED

**The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.**

*Diseases of the Chest: Diagnosis and treatment.* By Archibald R. Judd, M.A., M.D., thoracic surgeon for State of Pennsylvania, State Sanatorium, Hamburg, Pennsylvania, chief, department of thoracic surgery, Reading General Hospital, Reading, Pennsylvania, chief, department of thoracic surgery and consultant in bronchoscopy, St. Joseph's Hospital, Reading, Pennsylvania, and chief, departments of thoracic surgery, pulmonary diseases and bronchoscopy, Community General Hospital, Reading, Pennsylvania. 8°, cloth, 608 pp., with 140 illustrations. Philadelphia: F. A. Davis Company, 1947. $9.00.

*Histopathology of the Ear, Nose and Throat.* By Andrew A. Eggston, M.D., director of laboratories, Manhattan Eye, Ear and Throat Hospital, clinical professor of pathology (Post Graduate Division), New York University Medical College, director of laboratories, Mount Vernon Hospital, and pathologist, Harlem Eye and Ear Hospital; and Dorothy Wolff, M.A., Ph.D., research investigator, Endaural Hospital, New York City, and fellow in research, Harvard Medical School. 4°, cloth, 1080 pp., with 505 illustrations, 28 plates and 9 tables. Baltimore: The Williams and Wilkins Company, 1947. $18.00.

*Diseases of Children.* Edited by Donald Paterson, M.D. (Edin.), F.R.C.P., physician, Hospital for Sick Children, Great Ormond Street, and physician in charge of diseases of children, Westminster Hospital; and Alan Moncrieff, M.D. (Lond.), F.R.C.P., Nuffield Professor of Child Health, University of London, physician to out-patients, Hospital for Sick Children, Great Ormond Street, and physician, Children's Department, Middlesex Hospital. Vol. I, with material by twenty-nine contributors. Fourth edition. 8°, cloth, 771 pp., with 154 illustrations. Baltimore: The Williams and Wilkins Company, 1947. $9.00.

*A Prelude to Modern Science: Being a discussion of the history, sources and circumstances of the 'Tabulae Anatomicae Sex' of Vesalius.* By Charles Singer and C. Rabin. Publications of the Wellcome Historical Medical Museum. New Series, Number I. F°, cloth, 58 pp., with 59 illustrations. Cambridge: University Press, 1946.

*The Diagnosis and Treatment of Diarrheal Diseases.* By William Z. Fradkin, M.D., assistant attending gastroenterologist, Jewish Hospital of Brooklyn, physician-in-charge of Colitis Clinic, Department of Gastroenterology, and associate bacteriologist, Colitis Division, Department of Laboratories, Jewish Hospital of Brooklyn. 8°, cloth, 254 pp., with 114 illustrations. New York: Grune and Stratton, 1947. $6.00.

*Paravertebral Block in Diagnosis, Prognosis, and Therapy: Minor sympathetic surgery.* By Felix Mandl, M.D., professor of surgery, Hadassah University Hospital, Jerusalem. Translated by Gertrude Kallner, M.D. With a foreword by Max Thorek, M.D., professor of surgery, Cook County Graduate School of Medicine, Chicago. 8°, cloth, 330 pp., with 20 illustrations and 10 tables. New York: Grune and Stratton, 1947. $6.50.

## NOTICES

### ANNOUNCEMENT

Dr. Newman Cohen announces the removal of his office to 21 Bay State Road, Boston.

### NORFOLK DISTRICT MEDICAL SOCIETY

The Norfolk District Medical Society will meet at the Boston Medical Library, 8 Fenway, Boston, on Tuesday, November 25, at 8 p.m. A scientific program, entitled "Tufts College Medical School Night," consisting of five papers of general interest, will be presented by members of the faculty of Tufts College Medical School.

PROGRAM

Tufts College Medical School, Today. Dwight O'Hara, M.D.
Nephritis in Children. James Marvin Baty, M.D.
Cytochrome C and Its Therapeutic Possibilities. Samuel H. Proger, M.D.
Nitrogen Mustard Therapy in Hodgkin's Disease. William Dameshek, M.D.
Portacaval Anastomosis for Portal Hypertension. C. Stuart Welch, M.D.

This meeting is open to all physicians. A collation will be served.

### SUFFOLK DISTRICT MEDICAL SOCIETY

The Suffolk District Medical Society and the Boston Bar Association are sponsoring a series of medicolegal lectures, the first of which, entitled "The Doctor on the Witness Stand" will be given in Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Thursday, December 11, at 8 p.m. Judge Abraham E. Pinanski, of the Superior Court, will preside as moderator. Leland Powers, of the Boston Bar Association, will present the legal side, and Drs. Alan R. Moritz and Henry C. Marble will present the medical side.

All members of the Massachusetts Medical Society are cordially invited. Refreshments will be served.

### SUFFOLK DISTRICT WOMAN'S AUXILIARY

A meeting of the Woman's Auxiliary of the Suffolk District Medical Society will be held at the Boston Medical Library, 8 Fenway, Boston, on Thursday, December 4, at 2:30 p.m. The speakers will be Drs. Charles C. Lund and John F. Conlin. Tea will be served.

(*Notices continued on page xv*)